American Journal of Obstetrics and Gynecology

VOL. 30 ST. LOUIS, NOVEMBER, 1935 NO. 5

IN MEMORIAM

Barton Cooke Hirst

BARTON COOKE HIRST died September 2, 1935, at his home in Philadelphia, of acute dilatation of the heart. He was born in Chestnut Hill, Philadelphia, on July 20, 1861, the son of William Lucas Hirst, a prominent attorney, and Lydia Barton Cooke. The Hirst family tree is traced in England as far back as the twelfth century, and the American branch of the family springs from John Hirst, who emigrated and settled in Bethlehem, Pennsylvania, in 1749. The tradition of the family was the law, there having been generations of Dr. Hirst's forebears in Temple Bar, London, and his decision to study medicine was an early evidence of the independence of thought which was always a salient characteristic.

Dr. Hirst married Elizabeth Haskins Dupuy Graham of Philadelphia in 1890, who survives him, as do also a daughter, Mrs. Elizabeth Dupuy Graham Lippincott, and two sons, Barton, Junior, an aviator in the late War, and Dr. John Cooke Hirst 2nd, an obstetrician of Philadelphia. The third son, Thomas, a First Lieutenant in the 151st Field Artillery, died in action in the late War.

Dr. Hirst entered the College Department of the University of Pennsylvania from the Faires Academy with the class of 1882, but at the end of his freshman year, having made up his mind as to his life work, another example of his independence and early maturity, he entered the Medical School, graduating with the class of 1883. Subsequent to his graduation in medicine he served as an interne in the University Hospital and then studied in Heidelberg, Vienna, Berlin, and Munich, where he became an interne with *teaching* duties. This Munich appointment probably had a great deal to do with his lifelong fight for better teaching in obstetrics. At the time of this appointment, eighteen months after his graduation, from the highest type medical school in the United States, he personally had never confined a woman, while on the other hand many of the students whom he had to teach and direct had made deliveries in more than one case. It goes without saying that a man of his mental attributes could not but make an odious comparison between the teaching abroad and that in

the United States. In any event, we know that the practical training in obstetrics for students became one of the ruling passions of his life. When he returned to Philadelphia and was made an assistant to Dr. R. A. F. Penrose, then Professor of Obstetrics at the University of Pennsylvania, there was not a bed devoted to this branch of medicine in the hospital and no arrangements for extramural student obstetrics. As soon, however, as he was elected to succeed Dr. Penrose in the professorship, he filled both of these needs by establishing a maternity department in the hospital and by creating an extramural service for home deliveries by senior students under close supervision. This latter service was and is known as the Southeastern Dispensary. Until Dr. Hirst's retirement from the Undergraduate School he remained largely responsible for its financial support.

At the time of his election to the chair of obstetrics at the University in 1889 the medical faculty was probably the most famous in the history of the school. Agnew, Wood, Pepper, Piersol, Reichert, Norris, Leidy, Wormley, Goodell, Tyson, and White, form a company which might well have given pause to a new member whose life span at that time was twenty-nine years. That he was impressed, goes without saying, but by his sheer professional ability and his ever present tact he was able to make himself acceptable to all of them—no mean feat. It is noteworthy that Dr. Hirst was only the fifth man to hold this chair since the first incumbent, Dr. James, was elected in 1810, the others having been Dr. Dewees, who held it for only one year, and Drs. Hodge and Penrose. It may be said that four men—James, Hodge, Penrose, and Hirst—have divided the occupany of this chair for one hundred and seventeen years. Dr. Hirst occupied the chair of obstetrics in the University for thirty-eight years, delivering three lectures, or their equivalent, each week to crowded benches, and also personally conducting the large clinical service which he attracted to his ever growing department. The funds needed for new buildings were obtained to a large extent by his personal solicitation.

Dr. Hirst did a vast amount of gynecology as well as obstetrics in his service. He believed, taught, and fought for the interdependence of obstetrics and gynecology, at that time not generally conceded. In this movement he was a pioneer. He felt most strongly that no man unless a skilled pelvic surgeon could be considered a safe obstetrician, and that the reverse was also true, an opinion now almost axiomatic in the minds of those competent to judge, but at that time a very heterodox opinion in most quarters.

When he retired on age in 1927 from the chair of obstetrics in the Undergraduate School he was by far the oldest member of the faculty in point of service. The trustees of the University who in 1907 had conferred upon him the B.A. degree as of the class of 1882, and who subsequently gave him the honorary Doctor of Science degree, elected him, on his retirement from the chair of obstetrics, emeritus professor of obstetrics in the Undergraduate School, and on the amalgamation

of the Howard Hospital with the Graduate School of Medicine of the University, they elected him as professor of obstetrics in that institution with a service in the Graduate Hospital. He held this position until his death, conducting a very active teaching and operative service with the enthusiasm that was his in 1889, and with the ability and knowledge that his ripe experience had brought to full fruition.

Dr. Hirst held many and various positions in the medical world. He was proud to have been the Chairman of the Section on Obstetrics, Gynecology and Abdominal Surgery of the American Medical Association, and also to have been one of the founders of the American College of Surgeons. He was an enthusiastic member of the American Gynecological Society and one of its former presidents. He was a Fellow of the College of Physicians of Philadelphia since 1888. He was the only member of the Philadelphia Obstetrical Society ever to be elected three times as its president. He was a corresponding member of the Society of Obstetrics and Gynecology of Paris; Consulting Surgeon of the Paris Society of Foreign Surgeons; an honorary member of the Obstetrical Society of Edinburgh and also of the Belgian Gynecological and Obstetrical Society. The University of Pittsburgh gave him the honorary LL.D. degree.

His hospital activities in Philadelphia, aside from the University Hospital and the Hospital of the Graduate School of Medicine comprised staff membership formerly at the Philadelphia General and the Howard Hospital, and latterly until his death he was active on the staff of the Orthopedic and the Lying-In Hospitals. The writer always felt that his first and greatest love was to the Howard Hospital in which for many years he was the mainspring. In fact from the time of his election to the Howard Hospital until its amalgamation with the Graduate School of Medicine of the University it is no exaggeration to say that he was the most active member of its staff. It is a pleasure to bear witness to the fact that after the Howard Hospital had become an integral part of the Graduate Hospital Dr. Hirst transferred his allegiance to that institution.

In his earlier years he was a prolific writer. The *American System of Obstetrics*, edited by him, his *Atlas of Gynecology*, *Human Monstrosities*, as co-editor with Piersol, and his own two textbooks, the one on *Obstetrics* and the other on *Diseases of Women*, bear ample witness to this fact, not to mention his many scattered articles and papers.

Such is the imperfect record of his achievement, and truly it is an enviable one, but to the many who knew and revered him, it portrays but the shadow of the man himself. The writer had peculiar opportunities to appraise Dr. Hirst at his true value—first as his student, some years later as an assistant on his staff, and a quiz master under him, and for the past eight years as his colleague in the Graduate School of Medicine, and the attributes which have indelibly impressed

themselves were his modesty, his courtesy, his kindliness, which was unfailing, his interest in young men, his enthusiasm for the newer developments in medicine, his keen sense of humor, which made him enjoy a joke on himself at least as much as when another was the subject, an unusual trait, and his marvelous vitality, both physical and mental. Even during the past summer he followed his usual custom with regard to swimming, golf, and sailing; he continued to operate to the end of his life, and within two weeks of his death devised a new technic for sterilization.

As a consultant he was without a peer, not only in his knowledge but in his manifest sympathy with the patient and his meticulous courtesy to the physician. He was an omnivorous reader and a great sufferer from insomnia; this combination resulted in his being thoroughly conversant with general literature, and his interest in art and music must be emphasized. He was the life of the five o'clock social gatherings of medical men in the old days at the University Club before his particular *bete noire*, prohibition, put an end to them. In medical societies he was a most delightful essayist and his discussions of the papers of other men were always courteous, but he never hesitated to be critical when criticism was indicated.

He was a great teacher in the fullest meaning of that term, and in the opinion of thousands of undergraduate students of his day he was by far the best lecturer in the faculty. When it is remembered that actually several thousand men sat under him during his thirty-eight years of teaching, and that what he taught them has been utilized in their daily work among countless women patients, it must be felt that this alone would have been an enduring monument to his memory, even had he done no other meritorious work as a medical pioneer in obstetrical teaching and as a writer.

In his death, premature for him even at his age, medicine has lost an outstanding figure; obstetrics has lost one of the last of the pioneers, and his many friends and colleagues have an abiding sense of a loss which can only increase as time passes.

William R. Nicholson.

The Editors of the JOURNAL desire to add to the foregoing memorial an expression of their own sense of personal loss in the death of Dr. Hirst. He was a member of the Advisory Editorial Board from the time of its organization and during the earlier years in particular proved a good friend by his advice and counsel. Dr. Hirst occupied a unique position in the profession, he combined with his extensive knowledge of the science of medicine, a cultural and personal quality which is essential and most desirable in the equipment of a physician. He was a physician in whom the human side was of equal rank with scientific attainment. We pay honor to his memory.

George W. Kosmak.
Hugo Ehrenfest.

Original Communications

EXPERIENCE WITH MULTIPLE DOSE ROENTGEN THERAPY IN MALIGNANT DISEASES OF THE UTERUS AND OVARIES*

WILLIAM P. HEALY, M.D., NEW YORK, N. Y.

IN SEPTEMBER, 1932, at the annual meeting of the American Roentgen Ray Society, I gave as my opinion that any further improvement in statistics dealing with end-results in the treatment of cervical cancer by radiation would depend upon our ability to increase the amount of effective radiation reaching the cancer which already had invaded the parametria and at the same time to avoid doing serious damage to the normal tissues by the rays.

A review of the end-results published at that time by various well-established radiation clinics throughout the world indicated that substantially the same percentage of cures was obtained by all. It seemed evident, therefore, that the probable maximum percentage of cures had been attained by the methods of treatment then in vogue.

Interestingly enough, it did not seem to matter much just which plan of radiation therapy was favored by a clinic, as long as the maximum dosage of radiation, within the limits of normal tissue tolerance for adjoining structures, was given to the primary lesion. In the majority of instances this was accomplished by means of radium applied directly to the latter. In some clinics deep x-ray therapy was used in conjunction with radium, usually following it, although in a few clinics two cycles of x-ray were given, one preceding the radium applications and the other following them.

A study of the amount of effective radiation reaching the cancer located in the parametrial tissues by means of the methods of x-ray therapy in use at that time, readily demonstrated that the total dosage was so small as to be almost of negligible value as regards a destructive effect upon cancer, except in the presence of extremely radiation sensitive cancer growths. Its chief value seemed to be in the response obtained from the ulcerated and infected primary lesion which usually cleaned up remarkably under the x-ray so that the subsequent radium applications could be made more effectively and with less risk of local inflammatory reactions, or of causing severe and continuing infection and slough in the necrotic irradiated tissues.

*Presented at the Sixtieth Annual Meeting of the American Gynecological Society, held at Hot Springs, Va., May 27 to 29, 1935.

NOTE: The Editor accepts no responsibility for the views and statements of authors as published in their "Original Communications."

Actually, as far as treatment of cancer of the cervix was concerned, the only advantage accruing to clinics with well-organized deep x-ray therapy departments lay in the greater flexibility and range of treatment available for advanced cases and for cases in which one could not expect more than temporary palliation. Such patients stood the x-ray treatments well since it required but a few minutes to give each treatment. In this way the patients in the hopeless cases were probably given a few more weeks or months of useful life than could have been obtained by radium alone.

Accordingly with a view to increasing the amount of radiation reaching the parametrial field, we established a different plan of x-ray therapy in January, 1933, for our cases of cancer of the cervix. Our experience with the first 26 patients treated under this plan was given in a preliminary report read in September, 1933, before the American Congress of Radiology.[2]

We stated that "Our usual plan of external irradiation with x-rays was changed in order to increase the amount of effective radiation given to the pelvic field adjoining the cervix, with the thought of controlling the disease in advanced cases for a longer period of time, and possibly thereby to lead to an increase in the percentage of permanent cures in such cases."

The method followed in the 26 cases reported consisted in lengthening the target skin distance from 50 cm. to 70 cm. and in giving only 200 r. at one time to a skin field instead of 700 r. Lengthening the target skin distance increased the depth dose, and reducing the number of roentgens for each treatment diminished the skin reaction, thus permitting more treatments to be given to each field, thereby increasing the total number of roentgens given to each skin area. Daily treatments of 200 r. were given to each of two opposite fields until a total of 2,000 r. or in some cases 2,400 r. had been given to each of the four fields.

The x-ray dosage factors in this series were as follows: 200 kv. peak voltage, 30 ma. current, 70 cm. target skin distance, 0.5 mm. cu. + 2.0 mm. al. filtration, two anterior and two posterior fields, 10 × 15 cm. each, 200 r. per treatment.

A total of 400 r. were thus given daily to alternate halves of the pelvis including the corresponding half of the cervix. It required three to four weeks to give this series of treatments and when they were finished it was estimated that from three to five threshold erythema doses of roentgen radiation had been given to the cervix and parametria for a distance of 10 to 11 cm. lateral to the cervical canal. This was considerably more than had been obtained by our previous single cycle plan of 700 r. to each field at one exposure. The latter plan gave 1 to 2 threshold erythema doses throughout the parametria.

This first or experimental series was interesting and instructive to us in that the patients on the whole stood the treatments well. The skin

was not badly damaged, in fact only in 10 per cent was there a marked reaction with blistering and peeling. Bladder irritability except for temporary increased frequency was unusual. Intestinal disturbance was more constant. As a rule it was shown by diarrhea and cramps for a week or ten days but in a few instances these symptoms persisted longer and were more severe and caused in such cases considerable prostration and weight loss, nevertheless by hospitalizing such patients they were able to continue treatment.

We were favorably impressed by our experience with this series of cases and by the fact that in 20 of the 26 cases primary healing of the ulcerated, diseased cervix was observed under x-ray alone before radium was applied.

As our experience grew in the use of this so-called multiple divided dose plan of x-ray therapy, we found it desirable to vary the plan according to various controlling factors.

It was our impression that patients in poor or only fair physical condition did better under the single pelvic cycle rather than the multiple dose prolonged treatment plan.

Patients with very advanced disease in which treatment can be regarded only as palliative we believe should not be subjected to this intensive form of radiation therapy. A number of such patients were treated and gave a rather satisfactory and encouraging response for a few months, there was complete local healing with cessation of bleeding and discharge and a distinct gain in weight. After several months however local ulceration occurred again, the patients lost weight very rapidly and suffered intense pain from renewed cancer activity in the fibrosed parametrial tissue resulting from the roentgen radiation.

It is questionable in our minds whether one is justified in subjecting these patients, hopelessly ill with advanced cancer, to the mental and physical strain as well as the financial expense of prolonged radiation therapy when the probable prolongation of life will be so short and the ultimate pain and distress so great. As a result of our experience with such cases during the past two and a half years I have decided not to advise intensive roentgen radiation for them.

As a general proposition because of limited bed capacity in our hospital we prefer to carry on the x-ray treatments with the patients ambulatory and residing outside the hospital. If a patient's residence is more than forty-five to sixty minutes' journey from the hospital, we find it best to give only the single instead of the multiple dose cycle. Patients living near the hospital and in good physical condition may take a prolonged series of treatments. Those in poor condition or living at a distance must have a short series.

Patients with heavy pendulous abdomen or quite generally obese are not good subjects for roentgen radiation. Much skin and subcutaneous fat damage is apt to result, leading to localized areas of brawny indura-

tion with overlying telangiectases. Such areas are easily injured and this may result in chronic ulceration extremely difficult to heal. For these reasons roentgen radiation usually is omitted in obese patients. In re-

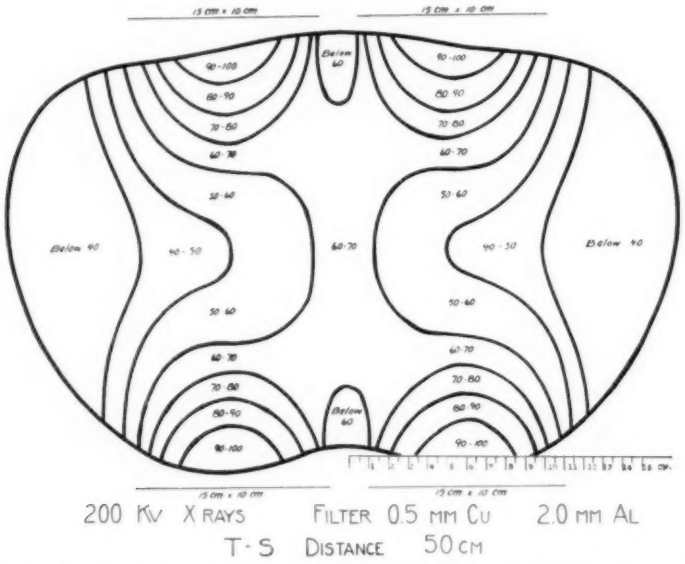

Fig. 1.—The distribution of roentgen radiation obtained within the average female pelvis from four fields of the size and location shown. Target skin distance 50 cm.

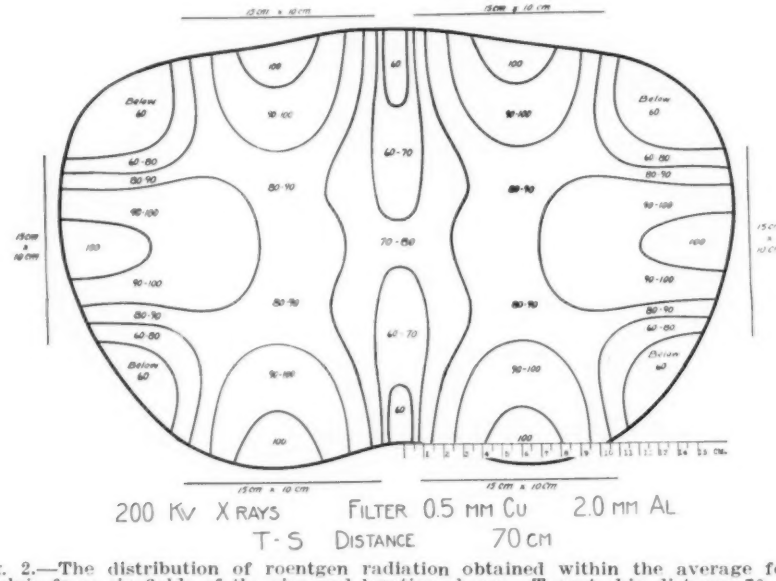

Fig. 2.—The distribution of roentgen radiation obtained within the average female pelvis from six fields of the size and location shown. Target skin distance 70 cm.

viewing our records for the past two and a half years, it is evident at once that these and other factors have guided or influenced us in our choice of the method of roentgen ray therapy for each case. Early in 1934 at the suggestion of Dr. A. Norman Arneson we added a right and a left lateral

pelvic field to the two anterior and two posterior fields previously used. This change was made in order to widen the field of parametrial radiation and to increase the percentage depth dose reaching the tissues in the outer portion of the pelvis.

With the previous set-up of four fields and 50 cm. target skin distance one obtained in the parametrial fields located from 6 cm. to 10 cm. lateral to the cervical canal about 50 to 40 per cent of the skin dosage. Under the new set-up of six fields and treatments given at 70 cm. from 85 to 95 per cent of the total skin dosage is obtained in these areas 6 to 10 cm. lateral to the center of the cervix. This is approximately an increase of 100 per cent in the amount of effective irradiation delivered to the outlying parametria (Figs. 1 and 2).[3]

At the present time, therefore, with few exceptions, all patients receiving roentgen radiation for carcinoma of the cervix are treated through six ports. From Jan. 1, 1933 to May 15, 1935, about 307 patients with carcinoma of the cervix were accepted for treatment. Most of these were primary cases, some were recurrent, a few were so-called prophylactic, following hysterectomy.

Eighty-nine patients received 1 or 2 cycles of 4 fields, 2 anterior and 2 posterior, 200 kv., at 50 cm., 0.5 cu., 2.0 Al., 700 r. each field. As a rule those in which only one cycle was given received it before the radium application and failed to return for the second cycle later on. The parametrial field in such cases therefore received the equivalent of about one threshold erythema dose from the x-ray. In the patients receiving two cycles one was given before and the other about four to six weeks after the radium, the parametrial fields received the equivalent of two threshold erythema doses from roentgen radiation.

Eighty-one patients received two cycles of six fields at 70 cm., 700 r. each, one cycle before and the other following the application of radium. In this group the parametrial tissues also received about two threshold erythema doses but the addition of lateral treatment ports widened out the parametrial fields so that a larger area about 10 by 16 cm. received the equivalent of two threshold erythema doses.

One hundred and seven patients received multiple divided doses of roentgen ray. The dosage factors were 200 kv., 30 ma. current, 70 cm. target skin distance, 0.5 mm. cu., 2.0 mm. Al. filtration, 14 by 10 fields, six fields, 2 anterior, 2 posterior, right and left lateral, 300 r. daily to each of two opposite fields for total of 600 r. daily.

Treatments continued until 1,500 r. to 1,800 r. had been given to each field. This would be equivalent to from 2½ to 3½ threshold erythema doses in a parametrial field measuring 10 cm. anteroposteriorly and 16 cm. transversely in an average female pelvis of 23 by 35 cm.

Those patients in whom an effort was made to give a long series of deep x-ray treatments are the ones with which we are chiefly concerned in this study as they are the cases in which the heaviest dosage was given by this method not only to the primary lesion and the parametria but also to the skin, the abdominal walls, the intestines, bladder, blood vessels, nerves, etc.

It should be of interest therefore to note the effect of such treatments on the cancer and on the normal tissues traversed by the rays, also to

determine whether these treatments can be safely given, and to ascertain if the response of the cancer to them is sufficient to justify the increased cost and inconvenience to the patient.

We fully realize it is not an innovation to give multiple divided doses of x-ray for the treatment of cancer. For a long time such treatments have been given by Coutard at the Radium Institute in Paris. While his method is best known because of his work with oral cancer, nevertheless he has also treated many of their cases of cancer of the cervix by means of multiple prolonged exposures to deep roentgen rays and has apparently led to a distinct improvement in the percentage of five-year cures reported by them.

In our work the effort has been made to continue the x-ray treatments in each case up to the limit of tolerance of the normal tissues in the irradiated fields. Since the percentage of radiation reaching the skin is always greater than that received by the underlying tissues we are usually guided in our decision to go on or to stop, by the skin reaction.

With the x-ray dosage factors used in our set-up, the threshold erythema dose is about 500 r. for a single exposure. Since six ports or fields are used and two opposite fields are treated daily, it requires three days to make one complete cycle of the pelvis. Therefore a seventy-two-hour interval elapses before the same skin area is treated again.

Duffy, Arneson, and Voke[4] in their study of human skin recuperation following irradiation concluded that the skin in forty-eight hours recovered 76 per cent of the immediate radiation damage suffered. They estimated that 425 r. would represent the threshold erythema dose for two treatments given at a forty-eight-hour interval. As our patients received only 300 r. every seventy-two hours to the same area with similar x-ray factors to theirs, there was sufficient time for marked skin recuperation between treatments.

With six fields we soon found that skin reactions and intestinal disturbances were more marked and appeared sooner than when only four fields were used. This no doubt is explained by the fact that only twenty-four hours elapse between the anteroposterior and lateral treatments on each side of the pelvis, and this results in cross firing of adjoining fields within twenty-four hours and a piling up of radiation effect in them.

Rarely, however, were the skin reactions alone severe enough during the course of treatment to necessitate postponing or stopping treatments. As it required fifteen to eighteen days to finish the x-ray, the skin changes were usually growing evident toward the end of the series and tended to be much more noticeable in the following two weeks after which time they rapidly subsided.

On the other hand disturbances of the bowel, evidenced by frequent stools and intestinal cramps might occur during the course of x-ray treatments and if not controlled by diet and medication would necessitate omitting the x-ray treatments for several days.

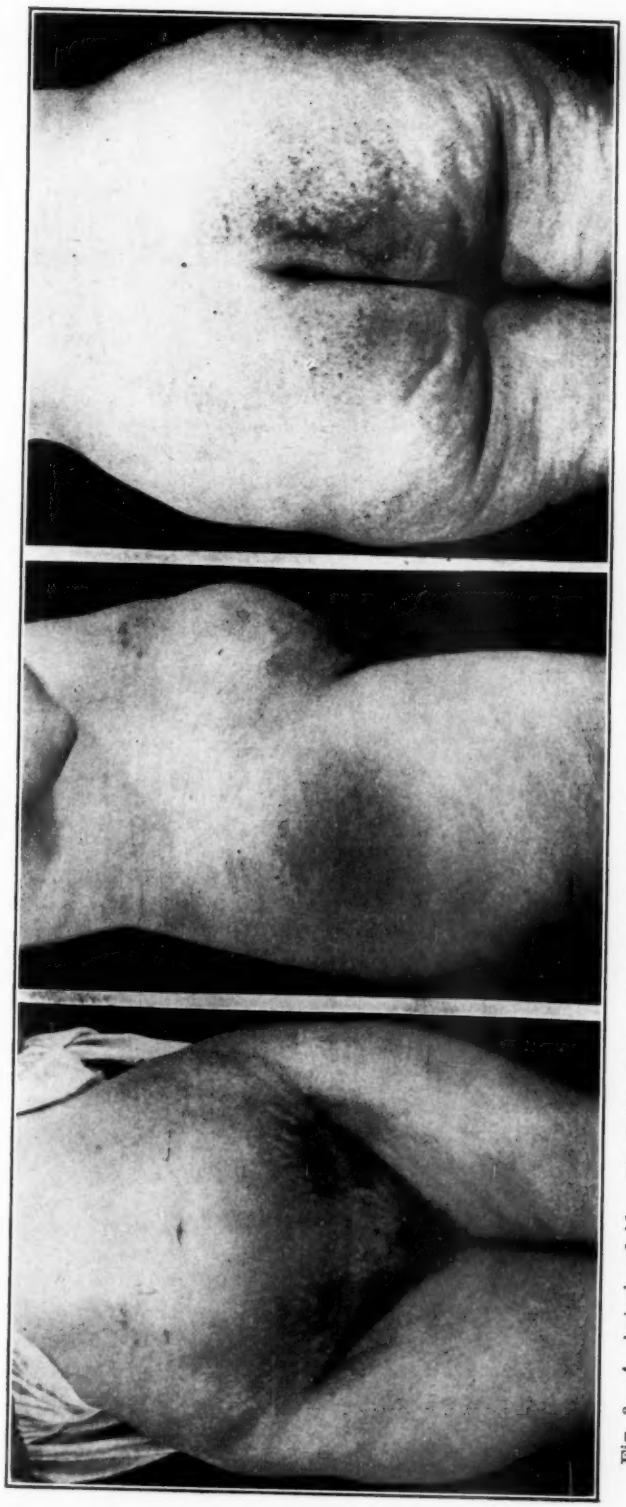

Fig. 3.—*A*, Anterior fields. Six fields, 70 cm., 300 r. × 2 fields daily, total 2100 r. each field. Average skin reaction, no blistering. Very advanced cervix case. Complete primary healing with x-ray. Radium tandem 3000 mc. hr. given one month later. Very satisfactory condition, one year later. *B*, Lateral fields. *C*, Posterior fields.

However it was more common to have the bowel symptoms make their appearance toward the end of the series, and then they might continue for two to four weeks afterward.

Bladder symptoms, if present at all, were usually mild and rarely required medication. It was not unusual to have a patient suffering from urinary frequency and dysuria caused by the cancer, remark that her bladder symptoms were relieved by the x-ray treatments.

Constitutional symptoms due to anorexia, nausea, vomiting, general prostration, rarely occurred. Strange to say the most severe constitutional, intestinal and skin reactions occurred in the cases in which the radium applications preceded the x-ray. This has been so noticeable in several cases in which x-ray therapy was started two or three days after the radium, because the lesions were not extensive and they were regarded as favorable for immediate application of radium, that I believe the x-ray series should not be started sooner than fourteen days after the termination of radium treatments. This will permit the tissues to recuperate somewhat from the intense reaction caused by radium before they are called on to take care of the x-ray treatments. Heyman[3] who gives a much smaller dosage of x-ray than we do, delays it until three weeks after the radium treatment.

In fact it seems to me quite definite that our advanced cases in which x-ray preceded radium were less disturbed by the combined x-ray and radium applications and went through all of their treatment more readily than the more favorable cases in which the radium treatment preceded the x-ray series.

If this observation is correct, I believe we will be justified in giving the x-ray series first in all cases in which it is to be used. The radium can be applied later.

In their preliminary report, Healy and Arneson[2] drew attention to the opportunity presented for frequent observation and study of the diseased cervix throughout the course of x-ray treatment. This is an advantage which should not be overlooked as it permits one to keep constantly informed as to the progress of the case and its response to radiation.

Dr. Fred Stewart of the Pathological Department who has kindly cooperated in this study by checking the radiation changes in the biopsy specimens, noted in some instances a slowing up in the regression of the cancer cells after a week or ten days of x-ray treatment. Thinking this might indicate greater resistance in the remaining cancer tissues, Dr. Stewart suggested increasing the x-ray dose per treatment in these cases rather than continuing with the same total daily dose throughout the series. In several cases a pyramidal plan of multiple x-ray treatments was followed.

This was a small series of 14 cases. Only 2 anterior and 2 posterior fields were used. The x-ray dosage factors were unchanged. Twelve

patients were given 5 pelvic cycles, 200 r. to each field, 2 opposite fields daily, followed by 5 pelvic cycles, 300 r. each field, 2 opposite fields daily, total r. to each of 4 fields at end of treatments was 2,500. Two patients were given 200 r. for 1 cycle, 300 r. for 4 cycles, and 400 r. for 3 cycles, total dosage to each field 2,600 r.

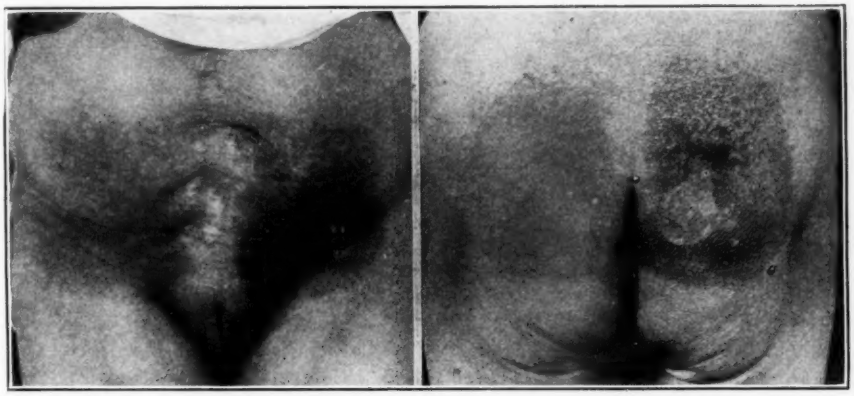

Fig. 4.—*A*, Anterior fields. Very advanced cervix carcinoma. Four fields at 70 cm., pyramidal method, 200 r. × 5= 1000 r., 300 r. × 5 = 1500 r., 2500 r. to each field. Marked dermatitis. Good primary regression. Photograph taken one week after last x-ray treatment. *B*, Posterior fields. Photograph taken one week after last x-ray treatment. Marked reaction with mild blistering and peeling.

Fig. 5.—*A*, Anterior fields. Patient V. Q., aged twenty-seven years, had advanced primary cancer of cervix. Six fields 14 by 10, 70 cm., 300 r., two fields daily. Total 1500 r. each field. Photograph taken one week after x-ray. Good skin reaction, no blistering. Complete regression primary lesion in five weeks. *B*, Posterior and lateral fields. Marked reddening and peeling, no blistering. Photograph one week after x-ray.

One patient in the first series stopped at 1,900 r. because of proctitis and one in the second series at 1,800 r. because of dermatitis. The disease, however, appears to have been controlled in both cases.

All the patients were suffering from advanced cancer of the cervix, 4 of the 14 were classified as very advanced. There were 4 colored patients in the group. With the two exceptions noted above the patients went through with their treatments without undue annoyance. Five of them

are alive and free from evidence of active disease, one has had fair palliation, four are doing badly and four are dead.

No conclusions can be drawn from this group except to say that 12 out of 14 patients or 86 per cent went through with this special form of x-ray dosage without undue difficulty. As to its ultimate value nothing can be said although it seems to offer interesting theoretical possibilities.

In reviewing the entire series of 307 cervix cases from the standpoint of unpleasant or distressing postradiation reactions there are two cases that stand out sharply from the others because of the extreme severity of their symptoms. Each was treated by vaginal and intrauterine application of radium and two days later in one case, three days in the other roentgen ray treatments were begun.

In the first instance a single pelvic application of six fields, 700 r. to each treatment, one treatment daily was given. In the second instance six fields were also treated, 300 r. was given daily to each of two opposite fields. This was continued until 1,500 r. had been given to each of the six fields.

Both patients had sharp skin reactions amounting to peeling and marked pigmentation. The bladder reactions were not severe but nevertheless were annoying. The intestinal disturbances were extremely severe and lasted for several months in each case. As a result the patients were badly prostrated and were bedridden for weeks.

In each instance the primary lesion quickly and completely regressed under treatment.

In both of these patients the radium treatments preceded the roentgen ray and the latter was started after a two-day interval in the first case and a three-day interval in the second case. I believe this is much too soon, especially if one has given a full tissue tolerance dose to the cervix with radium. The reaction to the radium will not have had time to assert itself before the additional effect due to the roentgen ray is added to it. It is probable that in many patients this will be more than the normal tissues in the radium treated field can stand, since they have already been subjected to the maximum dose by radium alone.

I believe we are working in the correct direction when we try to increase the amount of x-ray reaching the parametrial extensions of cervix cancer. The fractionated or multiple dose plan would seem to offer the best method of approach. It is evident that the greatest care has to be exercised in choosing the plan to be followed in each case. The multiple dose plan places much more responsibility upon the physician and the roentgen therapist and requires close supervision of the patient constantly during the treatment.

It is doubtful, however, if we can safely, with our present methods, increase the amount of x-ray reaching the parametria so that it will be effective in destroying metastatic squamous cancer, without at the same

time doing permanent and serious damage to the normal tissues and organs in the irradiated field. It is our impression that the lymph gland metastases of squamous epidermoid cancer are fully as radiation resistant as the primary lesion, if not more so.

At least 6 to 8 threshold erythema doses are required to establish regression of the primary lesion, therefore, it is reasonable to assume that as much will be necessary for control of metastases. Whether or not this amount of radiation could be safely spread over the intestinal field lying in the pelvis is questionable.

There is no doubt that we can improve upon our present technic by increasing still further the target skin distance and the filtration so as to eliminate as far as possible the soft gamma rays. At the same time it may be advantageous to reduce the daily dosage to 100 r. or 150 r. The difficulty with those changes is that they will greatly prolong the time of treatment for each case as well as the cost per patient. It will also reduce the number of patients who can be treated in a busy clinic.

The fractionated dose method we believe offers great opportunities for improving our therapeutic results by prolonging the lives of many patients one to two or more years and by curing a small percentage now lost because the radium and x-ray dosages previously used just failed to be sufficiently adequate to control their disease, especially in the parametrial tissues over an area within 6 cm. of the cervical canal. Even if we cure only three or four more patients in every hundred, it will be an increase of 10 or 15 per cent over our present salvage and the extra effort will be more than worth while. As was intimated above I do not believe we can hope, for the present, to save the lives of many patients in whom there is extensive or palpable disease in the more distant parametrial fields even with prolonged x-ray treatment of the fractionated or multiple dose type.

Our experience in the treatment of metastatic and recurrent ovarian cancer with multiple x-ray treatments has been more satisfactory.

For ovarian cases we use eight treatment fields, 4 anterior and 4 posterior, to cover the abdomen and pelvis, since the secondary tumors may exist any place within the peritoneal cavity.

The usual plan has been to give a treatment of 500 r. to one field daily. The pelvic fields are treated first and the upper abdominal fields next. The treatments are then repeated in the same order until 1,000 r. have been given to each field. This dosage does not seem to be excessive for these patients, although many of them are quite enfeebled by their disease and the presence of abdominal fluid in large amount which may require removal from time to time during the course of x-ray therapy.

The x-ray dosage given in this manner is equivalent to approximately two threshold erythema doses throughout the abdominal and pelvic fields.

Interestingly enough this rather small amount of radiation seems to be adequate to inhibit tumor growth activity in many cases and often

this is followed by complete disappearance of all secondary tumor masses. The primary tumor mass may also be considerably reduced in size but rarely disappears except in the case of anaplastic or embryonal cell tumors.

As soon as the tumor growths begin to regress under radiation, less ascitic fluid is formed, and, therefore, abdominal paracentesis is less frequently necessary. This is one of the first indications that the growths are responding to treatment.

When the patient responds favorably to the first series of x-ray treatments, we do not hesitate to repeat it in three months. At no time in our ovarian tumor cases have we had any unpleasant or serious skin or intestinal complications.

Our experience with deep x-ray therapy in multiple doses in ovarian tumors would indicate that such intraperitoneal metastases or implants are much more radiation sensitive than intraperitoneal metastases from uterine tumors. It is reasonable to assume that this may in part be due to the more delicate structure and high vascularity of the ovarian metastases, as against the more solid, less vascular metastatic squamous carcinoma of the cervix which often is encapsulated within lymph glands.

Some of the most striking cures which we have achieved were obtained by the use of x-ray in multiple divided doses in the treatment of apparently incurable cases of embryonal ovarian tumors in young women.

Our great disappointment has been our failure to control metastatic uterine cancer.

CONCLUSIONS

Our experience with multiple dose x-ray therapy for carcinoma of the cervix during the past two and a half years has been encouraging.

A satisfactory technic of x-ray dosage and treatment factors still needs to be developed.

Although we are at the present time giving 300 r. daily to two opposite fields we have not as yet determined that this is the optimum dose. Nor have we determined the optimum rate of administration.

The multiple divided dose method of x-ray therapy cannot be used to advantage for all cervix cases. It is desirable to choose with great care the cases in which it is to be used. By this method of careful selection, I believe, we will cure many patients who now die in the third and fourth years under our present methods of radiation therapy.

There is still much to be learned regarding x-ray therapy, and it offers an interesting and fruitful field for study and experiment.

REFERENCES

(1) *Healy, William P.:* Am. J. Roentgenol. **31:** 60, 1934. (2) *Healy, William P., and Arneson, A. N.:* Am. J. Roentgenol. **32:** 646, 1934. (3) *Arneson, A. N., and Quimby, E. H.:* Radiology **25:** 182, 1935. (4) *Duffy, J. J. Arneson, A. N., and Voke, E. L.:* Radiology **23:** 486, 1934. (5) *Heyman, J.:* Acta radiol. **16:** 129, 1935.

121 East 60th Street

PHYSIOLOGIC CHANGES OCCURRING IN THE URINARY TRACT DURING PREGNANCY*

J. Mason Hundley, Jr., M.D., Henry J. Walton, M.D., John T. Hibbitts, M.D., Isadore A. Siegel, M.D., and C. Bernard Brack, M.D., Baltimore, Md.

(From the Departments of Gynecology, Roentgenology, and Obstetrics of the University of Maryland, and the Department of Gynecology of the Johns Hopkins University)

FOR many years it has been known that dilatation of the kidney pelvis and ureter occurs during pregnancy. This observation, particularly as to its etiology, has been of special interest to obstetricians, urologists, and pathologists. Among the outstanding early investigators in this subject was Pierre Rayer, who, in his *Maladies des Reins* in 1841, called attention to the occurrence of dilatations in the urinary tract during pregnancy and the frequent presence of an associated infection. Another early observer was Cruveilhier, who showed in his *Descriptive Anatomy* 1843, that dilatations of the ureters occurred in all women who died following confinement or during the latter months of pregnancy. Due to the interest aroused by these findings, many men were stimulated to investigate the cause of these changes, and from then on, articles began to appear in the literature. Opitz, in 1905, presented a paper on "Pyelonephritis of Pregnancy and Puerperium" in which he stated that pyelonephritis occurs more frequently in the second half of pregnancy and is probably due to the compression of the ureter by the enlarging uterus at the pelvic brim, with subsequent dilatation of the urinary tract. With congestion thus brought about, infection may be established by organisms ascending from the bladder with the development of pyelitis or pyelonephritis. He was the first to advance the theory that pressure was the causative factor in ureteral dilatation with pregnancy.

In spite of the large amount of work done on the etiology of these dilatation changes, no one has yet, to our knowledge, been able to produce incontrovertible proof as to the cause of this condition.

Our interest was first aroused in this subject by the constant finding of marked dilatation of the pelvis and ureter in all cases of pyelitis of pregnancy. We were then of the opinion that these conditions were caused primarily by an infectious process with a subsequent development of these dilatation phenomena. From the information obtained from this investigation, we now feel that the dilatation and stasis come first and the infection is superimposed upon it.

*Read, by invitation, at the Sixtieth Annual Meeting of the American Gynecological Society, Hot Springs, Va., May 27 to 29, 1935.

In order to make a thorough study of the problem from every viewpoint, the following program of investigation was undertaken.

1. An intravenous urographic study of the urinary tract changes occurring in normal women during the succeeding months of pregnancy and the puerperium.

2. Obstetric observations of interest.

3. Investigation of urinary tract changes with the use of the indwelling catheter.

4. Urographic study associated with large pelvic tumors; pre- and postoperative manifestations.

5. Histology of the ureter during pregnancy.

6. Observations on the urinary tract of spayed dogs being subjected to prolonged injections of amniotin.

1. INTRAVENOUS UROGRAPHIC STUDY DURING PREGNANCY AND THE PUERPERIUM

Kretschmer and Heaney were the first to report in 1925, their observations on urinary tract changes during pregnancy by the use of retrograde pyelography. These investigators concluded that varying degrees of dilatation occurred in 80 per cent of normal pregnancies.

Three years later, Duncan and Seng contributed an exhaustive study of seventy-eight normal pregnant women who were examined by retrograde pyelography throughout the succeeding months of pregnancy and during the puerperium. The observations during pregnancy began at the sixth week and continued to term; whereas, the postpartum series began on the ninth day and continued to the twenty-fifth day. A summary of their conclusions is as follows: A dilatation of the right ureter was found in every case of pregnancy examined; whereas, the occurrence of right hydronephrosis was only slightly less frequent. The dilatation of the left urinary tract was not of such frequent occurrence. The multiparous woman showed these dilatation changes earlier, more frequently, and to a greater degree than did the primipara.

Every pregnant woman has some degree of obstruction with urinary stasis and resulting dilatation. A high percentage of normal pregnant and puerperal women have pus and "coliform organisms" in the urine.

With the introduction of intravenous urography, an increasing amount of investigative work has been done on the urinary tract during pregnancy. This safe and simple method of urography has been made possible by the pioneer work of Rowntree, Osborne, Sutherland and Scholl, working at the Mayo Clinic during 1923. They were the first to show that the renal pelvis and the bladder could be outlined following the intravenous injection of large doses of sodium iodide. However, it soon became evident that if this diagnostic method was to be universally adopted, a more tolerant substance than sodium iodide would have to be found. Through the efforts of Binz and Raeth of Berlin, a combination of iodine in high concentration with a pyridine ring was elaborated. Swick, in 1929, recognizing the possible value of this substance, known as selectan neutral, in pyelography, became associated with von Lichtenberg, and with the assistance of Binz, a nontoxic substance suitable for intravenous urography was developed. The substance was known as uroselectan.

Among the many investigators working on the urinary tract changes, Duncan and Seng, Lee and Mengert, P. Schumacher, Hofbauer, Dugald Baird, Kretschmer and Heaney may be mentioned.

It will suffice to briefly report the results of two thorough studies whose findings are generally similar to those obtained by other workers in this field.

Kretschmer, Heaney, and Ockuly, wishing to verify their results, reported in 1925, by the use of intravenous urography, studied thirty-one normal women throughout pregnancy and the puerperium, until the urinary tract had returned to normal. They also showed that as a rule the dilatation was progressive and that the presentation and position of the fetus showed no causal relationship to the dilatation or displacement.

Paul Schumacher (*Arch. f. Gynäk.* 143: 28, 1930), reports his observations on the study of one hundred normal pregnant women. He finds that during the first four months of pregnancy, the ureters preserve their normal course. During the fifth and sixth months in 50 per cent of cases, and during the seventh and eighth months in 80 per cent, there is an alteration in the direction of the lower part of the abdominal ureter. This is displaced outwards and backwards and comes to lie on the lateral slope of the psoas muscle and may have a convexity directed outward. The relations of the pelvic ureter show little disturbance by the growing uterus. Of the one hundred cases, there was a dilatation of both ureters in 83 cases, 15 of the right ureter only, and 2 of the left ureter only. The dilatation may reach a radius of 2 to 2.5 cm. and affects both primiparas and multiparas. Ureteral kinks were almost constantly found and were usually located just below the renal pelvis.

In order for us to make a thorough investigation of the dilatation phenomena occurring in pregnancy, it was necessary to study the changes throughout the entire course of gestation as well as in the puerperium. We were particularly interested in studying the causation of the ureteral changes and wished to test out some of the theories advanced, but we also wished to observe how soon deviations from the normal were noted, whether the dilatations were progressive and how soon retrogression took place.

It was decided that the closely related problem of pyelitis of pregnancy would not be taken up in this article but would be considered in a later publication.

For the sake of clarity, and in order to make certain deductions, it was decided to present and classify our findings according to three separate groups, namely: Stage 1: Changes occurring up to the fifteenth week of pregnancy; Stage 2: changes occurring from the fourth month up to delivery; Stage 3: changes during the puerperium.

This study was begun with thirty-five normal pregnant women who had no past history of any urinary infection, and whose urine was microscopically and culturally normal. However, for several reasons, such as development of nephritis early in pregnancy, pyelitis, failure to return, etc., eight patients were discarded, so that twenty-seven remained for a complete study. Of these, twenty were primiparas and seven were multiparas. Their ages ranged from sixteen to thirty-one years.

Through the generosity of the Winthrop Chemical Company, sufficient Neoskiadan, now known as Diodrast, was gratuitously supplied to make this study possible. The following was the method of procedure used. Twenty cubic centimeters of neoskiadan were slowly injected into the median basilic vein. The number of injections given in

all was 172, and at no time was a reaction of any consequence produced. If the solution was injected quite slowly, the only sensation experienced was that of diffuse body warmth; however, if it was given rapidly, the patient complained of nausea and at times vomiting occurred. The reactions were very transitory, lasting less than one minute. In two cases, some of the fluid was known to have escaped into the tissues of the arm during the injection, but no reaction of any kind developed. The first x-ray was taken fifteen minutes following the injection of neoskiadan, and subsequent exposures were made at fifteen-minute intervals. As pregnancy and dilatation changes in the urinary tract progressed, it was found that the excretion time was delayed and frequently a delay of thirty to forty-five minutes was necessary before a satisfactory film could be obtained. It was noted that the more marked the dilatation, the greater the delay in the excretion time; this resulted in the earlier appearance of the dye in the more normal side. Following delivery, it was necessary to take the first film as early as seven minutes after the intravenous injection, for if there was much delay, most of the dye was found in the bladder. This was due to the absence of urinary stasis, atony, and the return of the excretion time to normal. Urographic studies were made at intervals of six to eight weeks up to the time of delivery; they were then continued postpartum, until the urinary tract had returned to normal.

ANALYSIS OF RESULTS

Stage 1.—This portion of the study comprises examination of early pregnancies up to the fifteenth week. In this group there were thirteen patients examined, ten of whom were normal and only three showed slight changes in the urinary tract prior to the fifteenth week of pregnancy. Of these three, one examined at the ninth week showed dilatation, tortuosity and outward displacement of the right ureter. Another studied at the fourteenth week demonstrated dilatation of the right kidney pelvis as well as dilatation of both ureters. The remaining patient examined at the twelfth week showed the left kidney pelvis dilated.

Stage 2.—This period of investigation includes examinations from the fifteenth week of pregnancy to term. In this group there were twenty-seven patients studied and the following facts were brought out:

Dilatation of the pelvis and calyces of right kidney, 24 cases, 88.8 per cent.
Dilatation of right ureter, 25 cases, 92.8 per cent.
Dilatation of pelvis and calyces of left kidney, 6 cases, 22.2 per cent.
Dilatation of left ureter, 17 cases, 63.2 per cent.
Lateral displacement of right lumbar ureter, 7 cases, 25.8 per cent.
Lateral displacement of left lumbar ureter, 18 cases, 66.6 per cent.

Stage 3.—This final period of study began the seventh day postpartum and continued until the examinations showed a complete return to normal. All of the patients except one were examined during this period. The tabulated results follow:

On the seventh day postpartum, the urinary tracts of 8 patients had returned to normal.

On the tenth day postpartum, the urinary tracts of 2 patients had returned to normal.

On the fourteenth day postpartum, the urinary tracts of 3 patients had returned to normal.

On the twenty-first day postpartum, the urinary tract of 1 patient had returned to normal.

On the twenty-eighth day postpartum, the urinary tracts of 4 patients had returned to normal.

On the thirty-fifth day postpartum, the urinary tracts of 4 patients had returned to normal.

On the forty-second day postpartum, the urinary tracts of 3 patients had returned to normal.

On the fifty-sixth day postpartum, the urinary tract of 1 patient had returned to normal.

One patient was not examined following delivery.

From this study we find that the most constant change in the urinary system was a dilatation of the pelvis and calyces of one or both kidneys; a dilatation and tortuosity and kinking of one or both ureters, and a lateral displacement of these structures. Every case showed some deviation from the normal, ranging from a slight dilatation to a marked degree of hydronephrosis and hydroureter. The right kidney and ureter were affected more often than the left, but the left ureter was displaced laterally more frequently than the right. One of the most striking findings was that the portion of the ureter which runs over the pelvic wall was not visualized; whereas, the pelvic ureter was often well outlined. In not one of the cases was there found a definite and significant dilatation of the pelvic portion of the ureter. In Stage 1, examinations from the ninth to fifteenth week, there were thirteen patients studied and the pelvic ureter was visualized in all but one. Eleven of these showed some lateral displacement, while in two, slight tortuosity of the left ureter was noted. Only three showed slight dilatation of this pelvic portion of the ureter, two being on the right and one on the left. This latter finding is of special interest when considered in relation to Hofbauer's theory in regard to the etiology of ureteral dilatation.

With the advance of pregnancy, the dilatation of the ureter and pelvis gradually increased. We were unable to observe that the dilatation reached its maximum degree some weeks antepartum and then remained stationary until delivery. We feel that it is a gradually progressive dilatation.

Following delivery there is a return of the urinary system to normal. According to our findings and those of Duncan and Seng, the regressive changes do not seem to be so rapid as some authors state. We found that in twenty-six patients examined after delivery, eighteen of these showed a return to normal in twenty-eight days. However, one case required fifty-six days. These findings are somewhat similar to those of Duncan and Seng, who, in their postpartum study of thirty-six patients, found that from the ninth to the twenty-fifth day, a minority of the cases had returned to normal; whereas, a good majority still showed dilatation phenomena.

It is a well-known fact that the presence of frank infection greatly retards and delays the normal involution processes. However, these cases studied were normal and showed no signs of an inflammatory process.

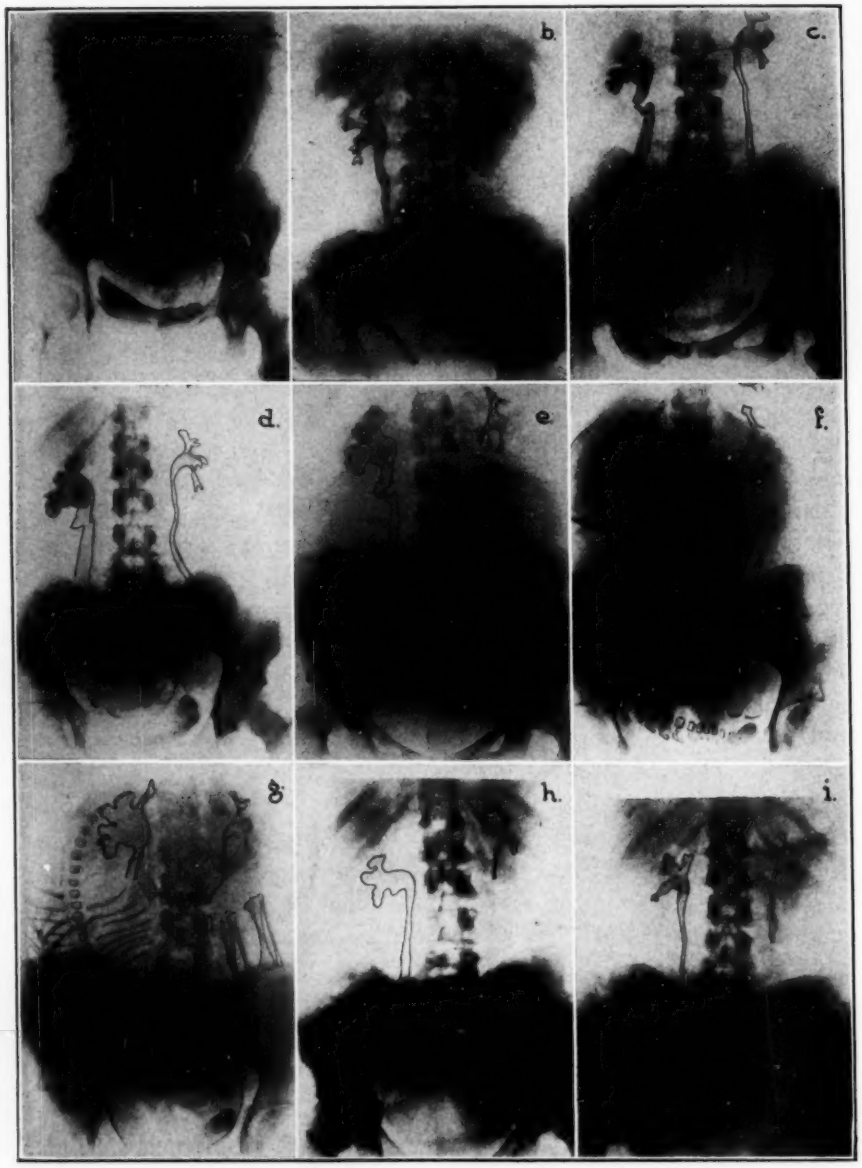

Fig. 1.—*a*, E. C. May 5, 1933. Normal pregnancy illustrating the distance between the head and the superior surface of the bladder. This has been a frequent finding and is not diagnostic of placenta previa.

b, A. P. Case 1. Fifteen weeks. Moderate dilatation of both pelves and lumbar ureters. Also slight dilatation of the right pelvic ureter. Fetus visualized in the pelvis.

c, M. L. Case 16. Eighteen weeks. Dilated pelvis and calyces of right kidney. Dilated and tortuous right ureter. Dilatation beginning at brim of pelvis. Slight dilatation of left lumbar ureter. Saucer-shaped depression of bladder. Fetus visualized in pelvis.

d, M. L. Case 16. Twenty-two weeks. Increasing dilatation of right pelvis, calyces, and lumbar ureter. Slight dilatation of left lumbar ureter with beginning outward displacement. Fetus well visualized in pelvis.

e, M. L. Case 16. Twenty-six weeks. No increase of dilatation of right pelvis, calyces, and ureter since last examination. Fetus visualized, breech presentation, spine to the left.

(Continued on opposite page.)

2. OBSTETRIC OBSERVATIONS

It was observed that the dilatation of the urinary tract occurred earlier in the multiparas than in the primiparas. All of the patients studied delivered normally, and there was no case of placenta previa found.

Early visualization of the fetus, during the routine study, was possible in most cases. In thirteen patients, the fetal skeleton could be demonstrated before the fifteenth week, three of these being seen by the tenth week. The position of the fetus changed very frequently, even during the later weeks of pregnancy. In only four cases was the fetus in the same position in the uterus in all examinations. At one x-ray examination, the fetus changed from a vertex to a breech presentation during the fifteen-minute interval between exposures. Owing to this frequent change of presentation, we do not believe that the fetal position has any bearing upon the dilatation changes observed in the urinary tract.

The presence of the placenta previa at times is extremely difficult to determine, and any safe procedure that would aid in the diagnosis of this anomaly would be greatly welcomed.

Menees, Miller, and Holly in 1930, introduced what they termed amniography, a method comprising the injection of strontium iodide solution, as a contrast medium, into the amniotic sac, through the abdominal wall and uterine wall, in order to show by x-ray the position of the placenta. They carried out their observations on twenty-one patients with no injurious or toxic effects to the mother or fetus in normal pregnancies. In one case of placenta previa, at the sixth month, the fetus was expelled about thirty hours after the injection.

Kerr and Mackay in 1932 carried out the same work using uroselectan B in place of strontium iodide, with no harmful effects on mother or fetus. They concluded that the position of the placenta could be determined by this method, but only patients in the latter weeks of pregnancy should be so investigated, as the injection predisposes to the induction of labor.

Recently, Ude, Weum, and Urner have described a roentgen finding which they think is diagnostic of placenta previa. They call attention to the following observation. With the advancement of pregnancy, the enlarging uterus presses down against the bladder, with a resulting concave, saddle depression of its superior surface. They have found that the instillation of a small quantity of sodium iodide into the bladder is helpful in its visualization. The diagnosis is dependent on the anatomical relationship between the fetal head lying in the lower uterine segment and the upper surface of the bladder. They state that the bony outline of the fetal head should be separated from the outline of the bladder only by the thickness of the uterine and bladder walls and the fetal scalp. In the case presented, they found the distance from the bony outline of the fetal head to the crescentic shadow of the bladder to

---

f, M. L. Case 16. Thirty-four weeks. Increasing dilatation of the right pelvis, calyces, and ureter. Left kidney and ureter appear normal. Fetus is visualized, breech presentation, spine to the right.

g, M. L. Case 16. Thirty-nine weeks. No increase of dilatation of the right pelvis, calyces, and ureter since last examination. Left kidney and ureter appear normal. Position of fetus: vertex presentation, spine to right.

h, M. L. Case 16. One week after delivery. The pelvis and calyces of the right kidney have returned to normal but there is still a moderate dilatation of the right ureter.

i, M. L. Case 16. Six weeks after delivery. The right pelvis, calyces and ureter are now normal.

NOTE: Urograms outlined for better reproduction.

be approximately 1 cm. This space was thought to be occupied by the placenta and a diagnosis of placenta previa was made and corroborated by cesarean section.

Our findings are not in accord with the above report. In ten of the twenty-seven patients studied, there was found a space between the shadow of the fetal head and the outline of the bladder which varied from 1 to 2.5 cm. in diameter. In none of the patients was placenta previa found, all having normal deliveries. Therefore, we do not feel that this finding is diagnostic of placenta previa (see Fig. 1, *a*, showing distance between fetal head and upper border of the bladder).

We now wish to present a series of illustrations depicting the varying changes in the urinary tract during pregnancy. Fig. 1, *b* shows beginning dilatation of the ureters and pelves of both kidneys at the fifteenth week of pregnancy. The following seven illustrations are succeeding examinations of the same patient, beginning at the eighteenth week of pregnancy and continuing until the sixth week postpartum (see Fig. 1, *c*, *d*, *e*, *f*, *g*, *h*, *i*).

3. INVESTIGATION OF URINARY TRACT CHANGES WITH THE USE OF THE INDWELLING CATHETER

Lee and Mengert in 1934 published an excellent article concerning the effect of pregnancy on the urinary tract. They investigated the debated question of pressure as the etiologic factor in the production of dilatation changes. They logically deduced that if these dilatations were produced by pressure, the relief of this pressure should allow the urinary tract to return to normal.

Their investigations were carried out on fifteen normal women in the last months of pregnancy. A retrograde pyelogram was done and the catheter allowed to remain in the ureter for a period of twenty-four hours, so that there could be continuous urinary drainage. In this way, the effects of stasis and back pressure from compression, if it existed, would be entirely relieved and the dilated tract would show definite evidence of returning to normal. However, none of their cases showed any decrease in dilatation by this continuous drainage for twenty-four hours. A number of intravenous urograms were then made on nonpregnant women who presented various types of pelvic pathology, including ovarian cysts, pelvic inflammatory disease, carcinoma of the ovary, and uterine fibroma. From their observations, they are "skeptical that ureteral obstruction, from any cause whatever, is the reason for dilatation of the upper urinary tract in pregnancy."

Being highly interested in the etiology of the dilatations occurring in pregnancy, we decided to repeat this work with the indwelling catheter and see if the results coincided. Our method of procedure was as follows:

Ten normal pregnant women during the last month of their gestation were selected for this study. An intravenous urogram was first done in order to determine which side showed the greatest degree of dilatation. This being decided, the patient was cystoscoped and a No. 9 x-ray catheter was introduced into that ureter which was the most dilated, the catheter passing as far up the ureter as possible. Specimens

and cultures were obtained and the pelvic capacity measured. Sodium iodide, 15 per cent, was then allowed to run in by gravity. On each examination, the top of the column of sodium iodide in the buret was kept at the same height above the level of the patient, so that conditions were similar in all cases. The catheter was then strapped securely to the abdomen. Liquids were forced and once every twelve hours 5 c.c. of silver nitrate sclution (1-1,000) were injected into the catheter, as a prophylactic measure. During the examinations of our first cases, the second pyelo-ureterogram was made twenty-four hours after the first; but we soon found that sufficient time had not elapsed to show regressive changes in the urinary tract. We discontinued the second x-ray at the twenty-four-hour interval and extended the time for the second pyelogram so that it was done forty-eight hours after the first. We now noticed that a definite diminution in the degree of dilatation of the pelvis and ureter had taken place. In several patients in whom the decrease of dilatation at the forty-eight-hour period was not absolutely definite, the catheter was left in situ for another twenty-four hours. With this additional period of drainage, the diminution in capacity became more marked. The rapidity with which the dilatation decreased varied in different cases, which observation coincided with the usual course of events following delivery.

ANALYSIS OF RESULTS

With continuous urinary drainage through the indwelling catheter for a period of forty-eight to seventy-two hours, a definite diminution in the size of the upper urinary tract occurred. It was found that drainage for a period of twenty-four hours was not sufficient to produce these regressive changes.

We were able to show a definite diminution in size of the dilated urinary tract in seven patients. In the remaining three, the following observations were made: In one, who delivered seven hours following cystoscopy, it was found impossible to introduce a catheter up the right ureter due to the pressure of the descending fetal head. One patient delivered thirty-six hours following the introduction of the catheter into the right ureter. The second urogram made at the first twenty-four-hour interval showed no signs of involution. However, the next retrograde pyelogram made twelve hours following delivery, the catheter having been reinserted, showed definite but early signs of a diminution of dilatation (see Fig. 2, *a* and *b*). The remaining patient delivered thirteen and one-half hours after the catheter was inserted. Through error, the indwelling catheter was left in situ during labor. On the following day, cystoscopy showed a line of hyperemic mucosa over the intramural portion of the ureter in which the catheter lay. This graphically illustrated the force exerted against the bladder by the descending head.

We will now show several urograms depicting the changes occurring in the urinary tract with prolonged urinary drainage.

R. G. (Fig. 2, *c*.) Base of pelvis measures 45 mm. Diameter of upper third of ureter is 11 mm. Diameter of middle third of ureter is 15 mm.

R. G. (Fig. 2, *d*.) Forty-eight hours later. Base of pelvis measures 35 mm. Diameter of upper third of ureter is 5 mm. Diameter of middle third of ureter is 11 mm.

H. R. (Fig. 2, *e*.) Base of pelvis measures 21 mm. Diameter of upper third of ureter is 14 mm.

H. R. (Fig. 2, *f*.) Forty-eight hours later. Base of pelvis measures 17 mm. Diameter of upper third of ureter is 9 mm. Diameter of middle third of ureter is 16 mm.

H. R. (Fig. 2, *g*.) Twenty-four hours later. Base of pelvis measures 16 mm. Diameter of middle third of ureter is 7 mm.

E. D. (Fig. 3, *a*.) Base of pelvis measures 5.2 cm. Diameter of upper third of ureter is 1.9 cm. Capacity is 46 c.c.

E. D. (Fig. 3, *b*.) Forty-eight hours later. Base of pelvis measures 4.5 cm. Diameter of upper third of ureter is 1.5 cm. Capacity is 40 c.c.

E. D. (Fig. 3, *c*.) Twenty-four hours later. Base of pelvis measures 4 cm. Diameter of upper third of ureter is 9 cm. Capacity is 21 c.c.

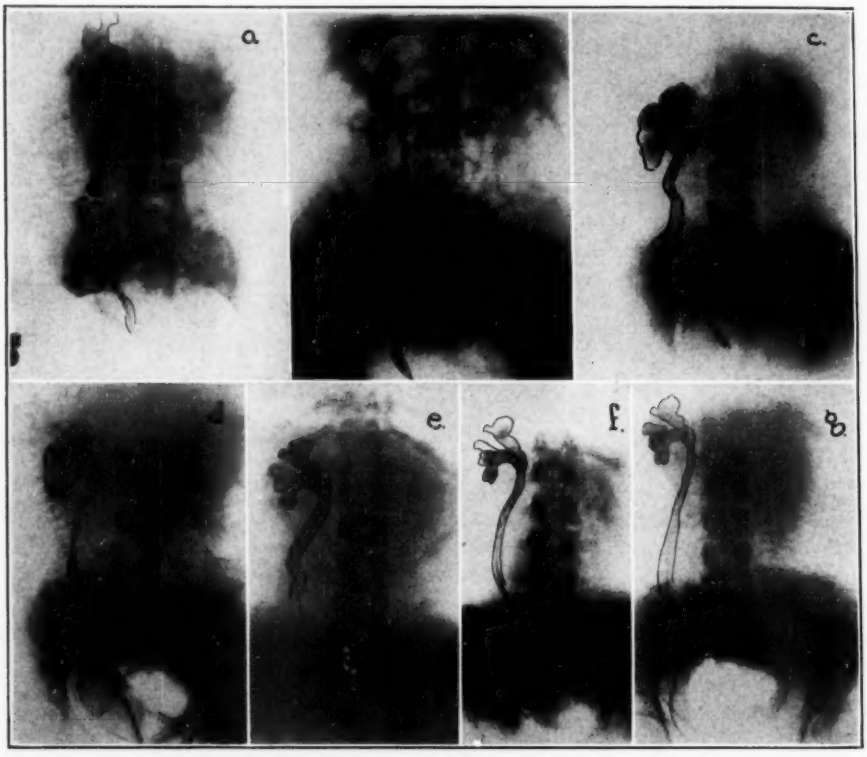

Fig. 2.—*a*, L. A. Jan. 19, 1934. Right kidney shows a marked hydronephrosis. Before delivery, the right ureter is dilated, nodular, and displaced laterally.
b, L. A. Jan. 23, 1934. Illustration twelve hours postpartum showing regression in the size of the pelvis, calyces, and ureter. No lateral displacement.
c, R. G. Indwelling catheter. April 4, 1934. Right kidney shows marked hydronephrosis and hydroureter. Indwelling catheter extending nearly to renal pelvis.
d, R. G. Indwelling catheter. April 6, 1934. In forty-eight hours, there is noted a definite regression in the size of the pelvis, calyces, and ureter.
e, H. R. Indwelling catheter. Dec. 17, 1934. The right kidney shows a moderate hydronephrosis. The right ureter is markedly dilated, tortuous, and laterally displaced. Indwelling catheter seen in upper end of ureter.
f, H. R. Indwelling catheter. Dec. 19, 1934. In forty-eight hours there is noted a diminution in size of the pelvis, calyces, and ureter.
g, H. R. Indwelling catheter. Dec. 20, 1934. Twenty-four hours later there is seen a still greater diminution in size of the pelvis and calyces.

4. UROGRAPHIC STUDY ASSOCIATED WITH LARGE PELVIC TUMORS, PRE- AND POSTOPERATIVE CHANGES

Having shown the changes that take place in the urinary system associated with pregnancy, we felt that it would be of interest as well as instructive to observe what effect, if any, occurred in the presence of pelvic tumors.

Recently, Baker and Lewis have reported their findings based on a comparative study of the urinary tract with pregnancy and also with pelvic tumors. They found

dilatation effects in all sixteen cases with large pelvic tumors, eight of which were ovarian cysts. They were of the opinion that mechanical pressure was the etiologic factor in the production of dilatation phenomena.

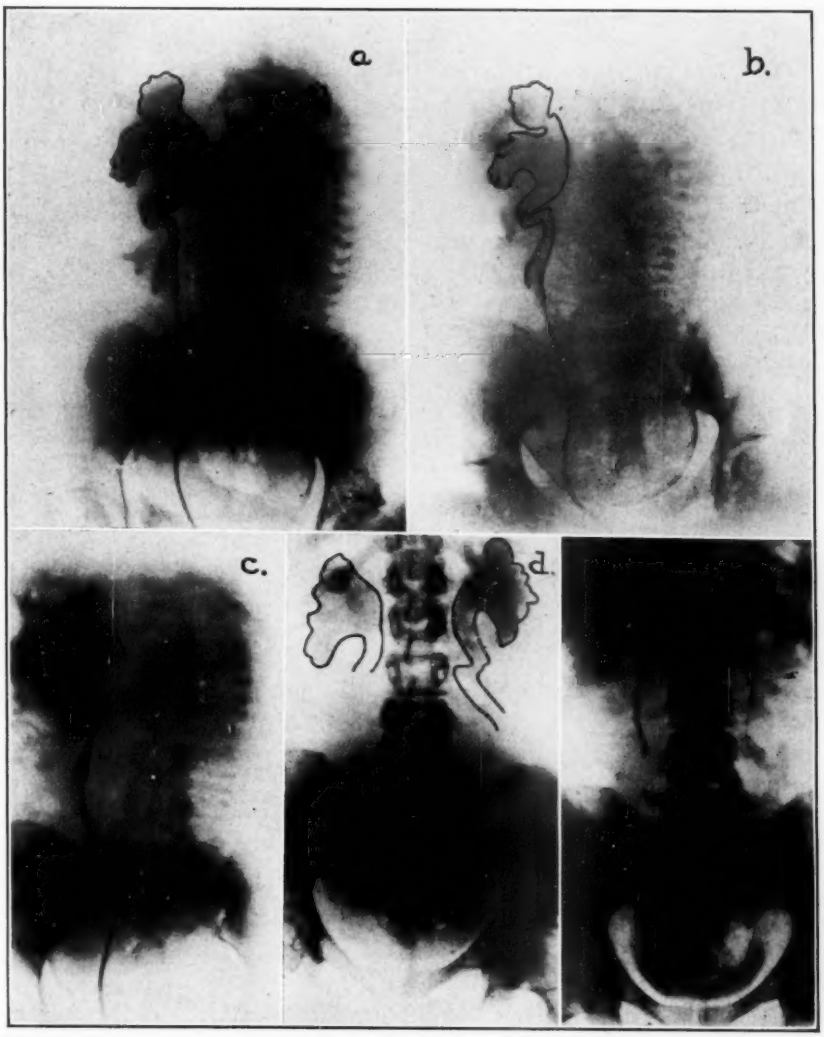

Fig. 3.—*a*, E. D. Indwelling catheter. Feb. 28, 1934. Right kidney shows a marked hydronephrosis and hydroureter, indwelling catheter tip being in upper end of ureter.

b, E. D. Indwelling catheter. March 2, 1934. In forty-eight hours, there is noted a moderate diminution in size of pelvis, calyces, and ureter.

c, E. D. Indwelling catheter. March 3, 1934. Twenty-four hours later there is noted an increasing diminution in the size of the pelvis, calyces, and ureter.

d, B. S. Feb. 11, 1935. Fibroid tumor filling pelvis, before operation. Marked dilatation of the pelves and calyces of both kidneys and both ureters.

e, B. S. March 21, 1935. (Thirty-eight days later) after operation. Pelves and calyces of both kidneys and ureters have returned to normal.

Our observations were carried out on a small series of large pelvic tumors, but sufficient in number to well illustrate what associated changes occurred in the urinary tract. Of the eight cases studied, six were large

fibroid tumors of the uterus, one an extremely large fibroma of the left ovary and the remaining patient had a fixed tumor which nearly filled the pelvis; on operation this proved to be a papillary carcinoma of the ovary. Every patient studied, with the exception of the one with the carcinoma of the ovary, showed dilatation effects in the urinary tract which were somewhat similar to those occurring during pregnancy. The main points of similarity were dilatation of the upper tract and delayed excretion time which returned to normal when the obstruction was removed. Intravenous urograms were made before and after operation. With the relief of pressure and the absence of urinary stasis due to removal of the tumor, it was remarkable to observe the resiliency and recuperative powers of the urinary tract. Figs. 3, *d* and *e* strikingly demonstrate how the urinary tract returns to normal. The patient of whom these films were shown stated that the pelvic mass had been present, to her knowledge, for at least three years. At operation, the spherical, fixed, uterine fibroma snugly filled the pelvic bowl and extended up to the umbilicus. It seems evident that pressure must be the cause of these dilatation changes, for here we have a dense pelvic tumor increasing in size and confined in an inelastic pelvis. And then witness the prompt regression of the tract after this obstruction has been removed. Of course, these tumors must be similar in size and contour to the pregnant uterus if they are to produce these dilatation effects.

5. HISTOLOGY OF THE URETER DURING PREGNANCY

During the past year, we have studied histologically the urinary tracts in thirteen women, all of whom excepting two died at term. One of these succumbed following an operation for ectopic pregnancy of six to seven weeks' duration. The other died at six months, of lobar pneumonia. This patient alone showed an infectious process in the urinary tract, multiple punctate abscesses being found in the cortex of the kidney. However, the bladder and ureters showed no evidence of inflammation.

In every case but one, some dilatation of the ureter was found, the right side being constantly more dilated than the left. It is frequently stated that the dilated, tortuous and kinked ureters occurring with pregnancy are longer than those not so associated. However, this has not been our observation. The longest ureter was found to measure 30 cm., and the shortest measured 17 cm. The average length was from 24 cm. to 28 cm. The sacculated dilatations of the upper ureter give one the impression that there is elongation of the tract, which is not borne out by actual measurement.

The gross appearance of the ureters associated with pregnancy had many points in common. As mentioned above, they all showed some degree of dilatation, usually on the right side, which always began above the brim of the pelvis. The lower end of the pelvic ureter was quite firm and rigid; whereas, the abdominal spindle was always flaccid and

ribbon-like, with definite loss of tone. In the upper part of this abdominal portion, one to three sacculations were observed which often were connected by delicate adhesions. There was no evidence of stricture formation made out either grossly or microscopically. The ureters were measured and sectioned at the following levels: Intramural portion, juxtavesical, midpelvic, brim of the pelvis, midabdominal spindle and the ureteropelvic junction.

In order to contrast the changes occurring during pregnancy with the normal, we studied as controls the urinary tracts of five women dying from other than urinary conditions. We also examined normal male ureters which differed in no way from the female ones.

In Bardeleben's *Handbuch der Anatomie des Menschen*, 1902, Disse has given an excellent anatomical description of the normal ureter and the following account is based primarily on his work. The lumen of this muscular tube is lined with stratified epithelium and when the organ is not dilated, folds of mucosa project into the lumen, giving a stellate appearance; these are absent when the ureter is distended with fluid or is dilated. The musculature of the ureter is composed of three layers comprising an inner and outer longitudinal and a middle circular. The muscle bundles are separated by interspaces which contain connective tissue fibers. The volume of the connective tissue is about equal to that of the muscle bundles. Throughout the abdominal portion of the ureter, the circular layer is well developed; whereas, the inner and outer longitudinal layers, especially the latter, are poorly defined.

The pelvic ureter is of somewhat different appearance. The muscular wall is more compact and with the increasing intermingling of the muscle fibers, it is difficult to distinguish separate layers. Here it is also noted that the muscle fibers lie next to the epithelium of the mucosa, for in this region, the tunica propria is absent. The longitudinal mucosal folds are not seen and the lumen often assumes the appearance of a "Y" formed slit. Just above the bladder in the adventitia, thick longitudinal muscle bundles, which apparently arise from the bladder, are seen. These bundles of muscle are surrounded by connective tissue and nearly encircle the ureter. It has been definitely shown that this structure, known as the ureteral sheath of Waldeyer, does not arise from the bladder but is a development of the outer longitudinal layer of the ureteral musculature. Multiple sections taken from different levels in the lower pelvic ureter show that these longitudinal muscle bundles extend up the ureter only for a distance of 3 to 4 cm. The adventitia about the lower end of the ureter is well developed, which gives added density and rigidity to this portion of the organ and is of great importance in binding the structures together.

In presenting our findings on the histologic changes occurring in the urinary tract during pregnancy, we are impressed with several observations which are constantly present, namely, hypertrophy of the musculature, edema and increased vascularity. These changes are noted in the urethra, trigone, bladder, ureter and kidney pelvis, and evidently go hand in hand with similar physiologic changes occurring in the generative tract during pregnancy. The most striking change seen in the urinary system is the marked hypertrophy of the ureteral sheath of Waldeyer. The degree of hypertrophy naturally varies but it is always present and is equally developed in each ureter. Hofbauer is of the

opinion that hypertrophic alterations in the musculature with hyperplastic changes in the connective tissue, plus the constricting tendency of the hypertrophic ureteral sheath, are essential factors in producing urinary obstruction with subsequent dilatation changes. This theory in relation to our findings will be discussed later.

Fig. 4, *a* shows marked hypertrophy of the ureteral sheath which nearly surrounds the lower end of the left ureter. The longitudinal muscle bundles are seen in the adventitia and are separated from the main muscular wall by a band of connective tissue. There is definite hypertrophy of the muscle fibers seen. However, at no time, in the many sections studied, were we able to demonstrate any new growth of tissue, either connective tissue fibers or nonstriated muscle fibers. Increased vascularity and edema were noted, with resulting loosening of the connective tissue meshes and separation of the muscle bundles.

A section taken from the juxtavesical portion of the right ureter of the same patient, Fig. 4, *b*, is quite similar to that just described. It is interesting to observe that in this patient, with equal development of the ureteral sheath in the lower ends of each ureter, there occurred a marked dilatation of the right ureter from the pelvic brim upward; whereas, there was no dilatation of the left ureter found. If the hypertrophy of the ureteral sheath were the etiologic factor, would there not be an equal dilatation of both ureters with the change occurring at the juxtavesical portion and not at the pelvic brim?

The following photomicrograph, Fig. 4, *c*, demonstrates an extreme degree of hypertrophy of the ureteral sheath.

In Fig. 4, *d*, the absence of hypertrophic changes in the ureteral sheath of a nonpregnant woman is noted. The longitudinal fibers making up the sheath are seen but are quite underdeveloped. The muscular wall is compact, no edema or increased vascularity is noted.

Fig. 4, *e*: Section shows another type of nonpregnant ureter at the bladder. In order to determine the origin of the longitudinal muscle bundles seen in the ureteral sheath, several blocks were taken from the intramural portion of the ureter and multiple sections from these studied.

Fig. 4, *f* very definitely shows that these fibers do not spring from the bladder but consist of the well-developed outer longitudinal muscular layer of the ureter. The ureteral wall is separated from the surrounding bladder musculature by an indefinite layer of connective tissue, making it difficult at times to determine the outer limits of the ureter. The mucosa is seen to be normal, there being no infolding of it in this region. The muscle fibers show the usual hypertrophy accompanying pregnancy and are seen directly adjacent to the epithelium of the mucosa due to the normal absence of the tunica propria in this location.

The next illustration, Fig. 4, *g*, shows the juxtavesical portion of the right ureter, the patient succumbing after an operation for an ectopic pregnancy of seven weeks' duration. There is a definite hypertrophy of the ureteral sheath seen, which demonstrates that as early as the seventh week of gestation, sufficient hormone is elaborated to produce this growth change.

We will now consider the abdominal ureter which, as already stated, differs somewhat from the pelvic portion. As we have shown, the abdominal spindle undergoes constant dilatation changes during the latter months of pregnancy, and reference to Fig. 4, *h* illustrates the findings in the ureter, diameter of which, taken at 14 cm. above the

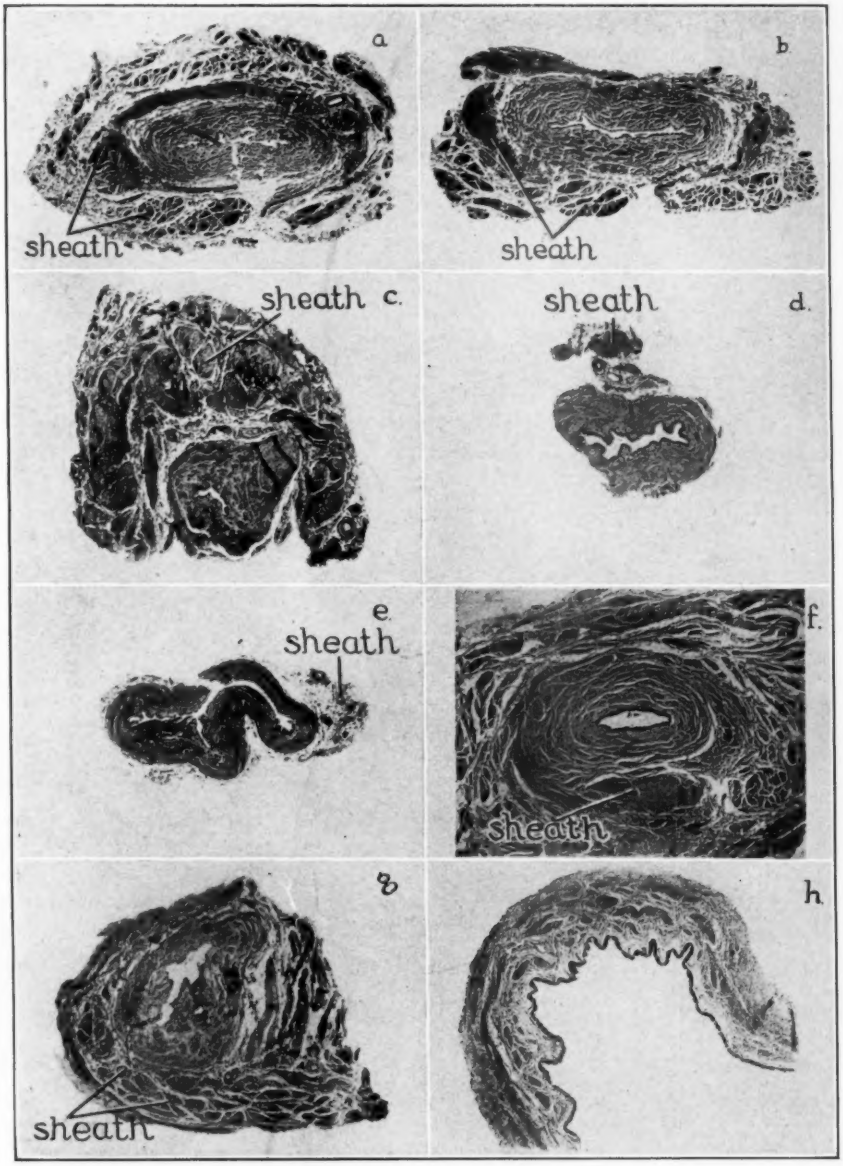

Fig. 4.—*a*, Pregnant ureter, left, at bladder, showing hypertrophy of the sheath of Waldeyer (×15).

b, Pregnant ureter, right, at bladder, same patient as *a*, showing hypertrophy of the sheath of Waldeyer (×15).

c, Another type of hypertrophied sheath of Waldeyer, associated with pregnancy (×15).

d and *e*, Different types of nonpregnant ureters, at bladder (×15).

f, Intramural portion of pregnant ureter, showing that sheath does not arise from bladder musculature (×35).

g, Hypertrophic sheath of ureter at bladder in patient with ectopic pregnancy of seven weeks' duration (×15).

h, Pregnant ureter, midabdominal spindle, 17 mm. in diameter (×35).

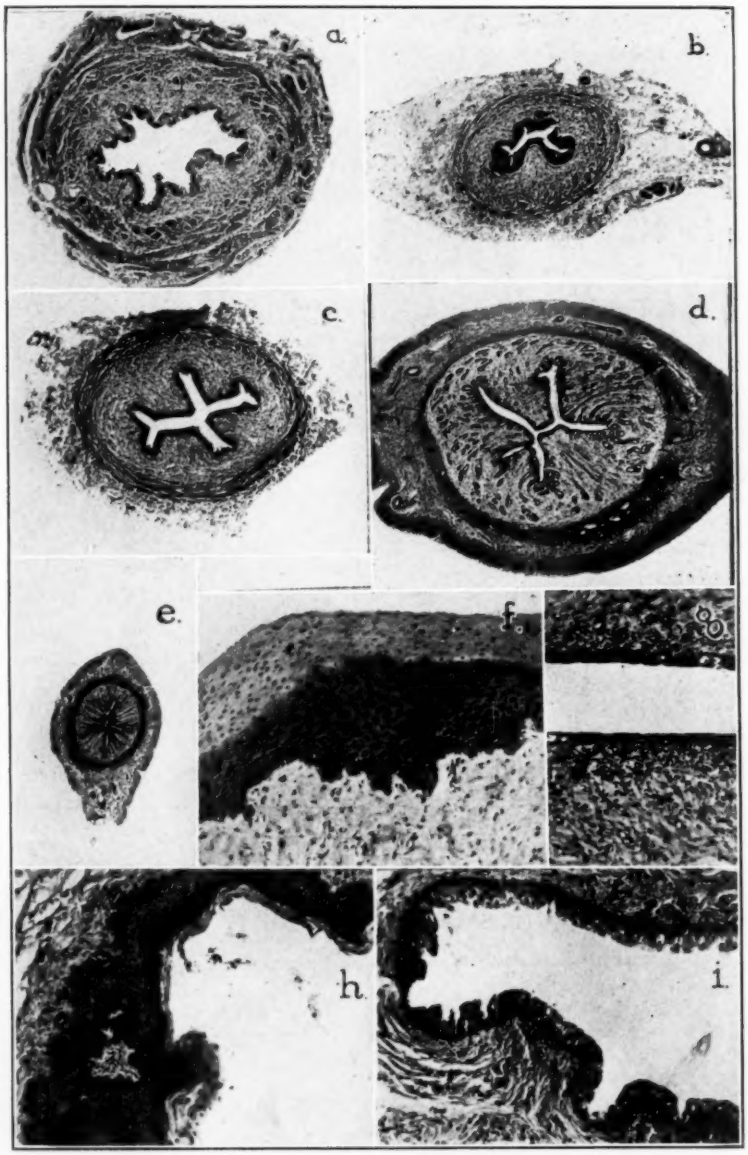

Fig. 5.—*a*, Nonpregnant ureter, midabdominal spindle. Note compact wall, high mucosa and no dilatation (×35).

b, Section of juxtavesical portion of dog's ureter, animal having been castrated and injected with amniotin. No definite change noted when compared with control (×15).

c, Control ureter (×15).

d, Uterine horn of castrated dog primed with amniotin (×15).

e, Uterine horn, control (×15).

f, Vagina of castrated primed dog showing marked growth effect (×140).

g, Vagina of control dog (×140).

h, Urethra of castrated, primed dog, showing mucosa changed to a squamous cell type with cornification (×140).

i, Urethra of control dog (×140).

bladder, is 17 mm., dilatation beginning at the brim of the pelvis. The wall of the ureter is thinned out; the mucosa is normal but quite low and there is some hypertrophy of the circular layer of musculature. The internal and external layers are seen but are not well developed. There is a good deal of edema present which separates the muscle bundles and also loosens the connective tissue fibers. In the wall of the abdominal portion of all of the pregnant ureters studied, there were found small collections of round cells, mostly confined to the tunica propria or adventitia. It was difficult to study mucosal changes for many of the sections showed autolysis and desquamation of the epithelial cells; and then, with dilatation of the lumen, the mucosa becomes very low, being only 2 to 3 cells high.

Fig. 5, *a* shows a fairly high magnification of a normal nonpregnant ureter in its midabdominal portion. The absence of muscular hypertrophy, edema and vascularity is to be noted. The circular layer comprises the major portion of the muscular wall.

Wishing to observe the dilatation changes occurring in the ureter when not associated with pregnancy, we were able to obtain hydroureters produced by metastatic parametrial masses from a carcinoma of the cervix. It was definitely shown that the dilatation changes were due to pressure exerted by the growing metastatic tumor in the parametrium. Microscopic examination of the intramural and juxtavesical portions of the ureter showed no evidence of obstruction at this location, although epidermoid carcinoma was seen surrounding the wall of the ureter. The section of the dilated ureter taken just above the brim of the pelvis showed edema of the wall which separated the hypertrophied muscle bundles one from another. Here, as in the pregnant ureters, the circular layer comprised the major portion of the muscular wall. In this case, the hypertrophy is produced by the increasing muscular effort of the ureter in its endeavor to expel urine through its partially obstructed lumen. This is an example of work hypertrophy.

During the investigation of the urinary tract with pregnancy, the examination of the trigone revealed definite hypertrophy of the muscle layers associated with edema and increased vascularity. It was difficult to definitely determine if hypertrophic changes also occurred in the bladder, as the size of the muscle bundles vary greatly, depending on the bladder being contracted or distended. However, we believe that hypertrophy of the musculature does take place.

At this point, we wish to make a few remarks in regard to the cystoscopic findings during pregnancy. We find that the most satisfactory method of cystoscopy in the presence of pregnancy is the Kelly method, in which the patient is in the genupectoral position, thus permitting an excellent view of the fully distended bladder, made possible by

the dropping away of the enlarged uterus. The urethra is found to be soft, vascular, and quite easily dilatable. The bladder mucosa at the base is usually slightly hyperemic, while the trigone gives an even more injected appearance. It is frequently said that the distance from the internal urinary meatus to the ureteral orifice is increased, as is also the length of the interureteric ridge. One is impressed by the fact that the orifices always seem much higher up in the bladder and more laterally displaced during pregnancy. However, actual measurements, compared to the controls, showed no increase in the size of the trigone. It is probable that the urethra is somewhat elongated by the growing uterus, which would account for the apparent change.

Another observation of interest which we frequently have found is that when a catheter, armed with a 4 mm. wax bulb, is introduced up the ureter during the latter months of pregnancy, obstruction is met with at the brim of the pelvis, and on withdrawal, there is considerable "hang" encountered at this same point. However, if this procedure is carried out shortly after delivery, the obstruction and "hang" have completely disappeared. This would indicate that whatever obstruction had been present during pregnancy has now been removed by the birth of the child. It would seem that these observations would support the theory of pressure as the etiologic factor in the production of dilatation.

Carson, in his autopsy study of ureteral dilatation of pregnancy in sixteen cases, found constant dilatation of the right ureter with changes in the left nearly as frequent. He states that pressure against the ureter produces dilatation and with the introduction of pyogenic organisms, an inflammatory reaction may develop, with the formation of scar tissue and resulting stricture. One of the three patients, in whom he found inflammatory strictures, I had treated for a severe pyelonephritis with no avail, necessitating the termination of the pregnancy at the thirty-fifth week. Unfortunately, the patient died and autopsy revealed a definite stricture, measuring 4 to 5 cm. in thickness, situated 6 cm. below the ureteropelvic junction.

Our histologic studies were made, as far as we could determine, on normal urinary systems, and as above mentioned, no evidence of stricture formation could be made out. Duncan and Seng, in their series of 156 ureters studied, stated that one stricture of the ureter was found.

Dugald Baird, in an exhaustive autopsy study of the ureters in 102 women during pregnancy or within a few days following delivery, found ureteral dilatation of very common occurrence, 85 per cent in the right urinary tract and 72 per cent in the left. He confirms the observation first made by Hofbauer concerning the hypertrophy of the ureteral sheath during pregnancy, and he is of the opinion, from studies made on the living at the time of cesarean section and on undelivered women at autopsy, that the ureter can be compressed between the uterus and psoas muscle on the right side. We have also observed at autopsy how readily the exposed right ureter at the pelvic brim can be compressed by the enlarged uterus, and we feel that this is a causative factor in the production of dilatation.

6. OBSERVATIONS ON THE URINARY TRACT OF SPAYED DOGS, BEING SUBJECTED TO PROLONGED INJECTIONS OF AMNIOTIN

From a survey of the literature and the differences of opinion that exist as to the etiology of ureteral dilatation, it is evident that the question is complex and that several factors may play a rôle in its production.

From our study of the urinary tract in pregnancy, we find that dilatation changes occur as early as the fifteenth week when the growing uterus is rising out of the pelvis. The ureter soon becomes dilated, tortuous, and sacculated, and there is a decrease in its rhythmical expulsive force due to loss of tone. This atony affects the entire ureter with the exception of its lower portion where it is reinforced by the ureteral sheath. The examination of the ureter in the patient dying following the ectopic pregnancy of seven weeks' duration showed definite hypertrophic changes of the ureteral sheath, as well as an increased vascularity, softening and atony of the abdominal ureter. It is this preliminary atonic change which allows the soft, pregnant uterus to compress the ureteral wall, with a resulting dilatation. The degree of dilatation and tortuosity is not nearly so marked in the presence of an impacted, dense fibroid of years' duration. These atonic and hypertrophic manifestations must be the result of hormonal activity elaborated by the process of pregnancy.

When one considers that the generative and urinary systems arise embryologically from the same anlage, and that the ureter is a budding off from the wolffian duct, it is not too speculative to deduce that the same hormones incidental to pregnancy, which produce gestational changes, would also affect the urinary system. We know that during the progress of pregnancy, large quantities of anterior pituitary sex hormone and estrin are found in the urine. The luteinizing substance designated as prolan by Zondek and Aschheim, reaches its maximum excretion of 5,000 to 6,000 M. U. per liter of urine during the fifth month of pregnancy; whereas, the excretion of estrin in the urine during early pregnancy is quite low, and ascends to its maximum of 10,000 to 40,000 M. U. per liter in the last month of gestation. Following delivery, there is a precipitous fall in the quantity of estrin excreted, which is due to the loss of its main source of supply, the placenta. Iscovesco, in 1912, showed that this organ contains large quantities of this growth substance, and now, estrin for therapeutic use is largely obtained from the placenta and amniotic fluid of cattle. As prolan is free of the growth promoting hormone, and as estrin is capable of producing growth, vascularity and edema in the generative tract of a spayed mouse, it is possible that this growth producing substance, estrin, is directly responsible for the muscular hypertrophy and vascularity in the trigone, bladder and ureter.

With the termination of pregnancy, the regressive changes in the urinary tract seem to go hand in hand with those occurring in the generative system.

Mengert has investigated the effect of pregnancy upon the ureters of common animals, using forty-two mammals of eight species, half of which were pregnant and the others being used as controls. The series examined included the cow, macacus monkey, dog, cat, rabbit, guinea pig, hog, and rat. In brief, a summary of his findings is as follows: There was no dilatation of the ureter found in any of the pregnant animals examined. A significant increase in the proportionate area of the ureteral sheath was noted in the monkey and the cow, and a significant decrease in the rabbit. The ureteral sheath does not seem to follow any set rule with regard to pregnancy. There was no significant hypertrophy of the circular musculature and the mucosa did not show any increase in the number of cell layers or in the size of the individual cell elements. He concludes from his observations that pregnancy has no effect upon the ureters of the animals studied.

On reviewing his work on the average area of circular musculature of the juxtavesical portion of the ureter of the different pregnant and nonpregnant animals, it was noted that only the dog, monkey, and hog showed an increased area of musculature during pregnancy; and only in the dog did the change seem significant. Mengert felt that this change lost its significance when it was observed that the pregnant animal weighed twice as much as the control.

In view of this finding, we thought it would be of interest to see what changes, if any, would occur in the urinary tract of a spayed dog after prolonged injections of amniotin. The following investigation was then undertaken.

Six healthy, medium-sized female dogs were selected, two of which were castrated, and on one an exploratory laparotomy was done to definitely rule out pregnancy; the ovaries were not disturbed. These three animals received daily injections of amniotin in oil,* until each had received a total of 5,250 R. U., the daily dose being 100 units. For each of these injected animals there was a control, two being castrated and the remaining one was a normal control for the noncastrated injected animal. The injections were begun on February 18, and eighteen days later, bleeding from the vagina began. This was noted in the two castrated dogs; however, the remaining one which had not been castrated did not show bleeding until eight days later. We had contemplated giving the amniotin over a period of seventy days, which is approximately the time of gestation in dogs; however, distemper broke out in the kennel, so on the fifty-third day we decided to end the experiment before the animals became seriously affected. The dogs were then autopsied.

The gross description of the genitourinary organs follows: The uterus and vagina of the injected animals showed, as was expected, marked enlargement when compared to the castrated controls. The length of the vagina was not changed by the hormone but there was a marked thickening of the wall, 8 mm. as compared to 3 mm. There was no variation in the length of the ureters and there was no marked change in their diameters. The ureters were carefully measured at the bladder, in the midabdominal portion and at the ureteropelvic junction. The average variation of the diameters was between 1 and 1.5 mm. The diameters of the castrated controls measured 2 to 2.5 mm., whereas the animals that were castrated and injected measured 3 to 3.5 mm.

*Supplied through the courtesy of E. R. Squibb and Sons.

Microscopic Findings.—There was no significant variation in size or structure found between the ureter of the stimulated dog and its control. There was no apparent change in the musculature or in the connective tissue. The mucosa was of the transitional type and showed no evidence of a change to squamous epithelium. Several of the dogs showed clumps of lymphocytes in the submucosa. None of the sections showed definite dilatation of the lumen. Fig. 5, *b* shows ureter of castrated injected dog at the bladder. Fig. 5, *c* shows ureter of castrated control at the same level. The ureter of the control is definitely larger than that of the injected castrated dog. This finding loses its significance when we realize that the control dog weighed ten pounds more than the injected animal. The uteri of the three castrated animals which received the hormone showed similar hypertrophic change. The uterine walls were much thicker, due to the increase in size of the muscle layers and the individual muscle fibers. Fig. 5, *d* shows section of uterine horn of castrated injected dog. Fig. 5, *e* shows section of uterine horn of castrated control. However, the most striking change was in the endometrium. This structure showed great thickening, vascularity, and loosening of the stroma. The main change was seen in the glands, which were longer, more dilated, and slightly tortuous. No evidence of secretion was made out. The epithelial cells lining the glands were of the high columnar type with the nuclei occupying the basal position. The uterine changes in the noncastrated injected dog showed hypertrophic changes but not so marked as in the ones just described. The uteri of the castrated controls were very small and atrophic, the stroma compact, and the mucosa very low.

The vagina of the stimulated, spayed dog showed the usual changes of estrus, the mucosa consisting of a thick layer of stratified squamous epithelium. The superficial half was composed of pale staining cornified cells; in the deeper portion, dark blue staining epithelial cells, which grew downward in numerous papillae, were seen. The wall of the vagina showed marked proliferative changes when compared to that of the control (see Fig. 5, *f* and *g*, for comparison).

In the routine examination of the organs, there was noted a marked change in the urethral mucosa. This structure normally shows transitional epithelium, the surface cells being cuboidal in type. However, the mucosa of the castrated dogs that received the hormone was changed into a typical stratified epithelium. The mucosa was definitely thickened and its superficial portion consisted of pale staining, cornified epithelial cells, similar to those seen in the primed vagina. The basal portion consisted of deep blue staining cells with papillary downgrowths. The muscle bundles showed no evidence of hypertrophy (see Fig. 5, *h* and *i*). The urethral section of the castrated control showed the usual low transitional type of epithelium.

In summarizing the results obtained from this short study, we find the following: There was no significant change observed in the ureters of the castrated injected animals as compared to the castrated controls. A marked growth of the uterus and vagina was obtained with definite hyperplasia of the endometrium and cornification of the superficial vaginal epithelium. In the urethra of the stimulated animals, the transitional epithelium was changed to a definite stratified type with cornification of the surface epithelium.

These investigations will be continued, for it is impossible to draw any definite conclusions based on such a small series of observations.

ETIOLOGY OF URETERAL DILATATION

We have shown by this investigation that some degree of dilatation of the urinary tract occurs with every pregnancy. The right side is

affected much more frequently than the left, and the dilatation invariably begins at the brim of the pelvis.

The cause of this dilatation is dependent upon two primary factors, namely, first, a softening process in the ureter due to hormonal activity, and second, pressure exerted by the growing uterus upon the ureter at the brim of the pelvis.

We have seen that early in pregnancy certain changes in the urinary tract become evident. The wall of the abdominal ureter becomes softer, flaccid, and atonic. Associated with this softening process, hypertrophic changes become noticeable throughout the ureter. The most striking change was noted in its lower end, where there was marked hypertrophy of the ureteral sheath of Waldeyer. The rest of the ureter also participates in this hypertrophic development but not to such a marked degree. The circular musculature of the abdominal spindle was the most involved. We have seen that at the seventh week of pregnancy, definite hypertrophic changes are present in the juxtavesical portion of the ureter, associated with increased edema and vascularity.

When we consider that the generative and urinary systems arise embryologically from the same anlage, it does not seem too hypothetical to reason that the hormones elaborated during pregnancy might have some effect upon the urinary system. It would seem most logical to deduce that estrin, which is elaborated in enormous quantities during pregnancy and produces vascularity, edema, hypertrophy, and swelling of the generative tract, could produce a similar change in the urinary tract.

In support of our hypothesis of hormonal activity upon the ureter, we present this very interesting case. We were fortunate in obtaining the urinary tract of a patient dying from a tumor of the testicle with generalized metastasis. The following is a description of one of the metastatic masses occurring in a lymph node. There are seen many tumor masses separated by fibrous tissue bands, into which, in several areas, fresh hemorrhage has occurred. In some areas the tumor is necrotic. In its well-preserved portions it consists of cells which resemble epithelial cells. The nuclei are irregular in size and shape and vary in intensity of staining. The cytoplasm is drawn out into long strands which interlace and surround small spaces. There are numerous masses of pink-staining material which vary in size and are undoubtedly syncytium. Imbedded in them are numbers of Langhans cells with irregular, very deep staining nuclei which vary greatly in size and shape, but are usually ovoid in form. The diagnosis of chorionepithelioma was made (see Fig. 6, *a*). In the testicle removed at operation, no definite chorionic epithelium was seen; however, the urine was strongly positive for prolan on two occasions. The examination of the ureter showed definite hypertrophic changes throughout the whole ureter but was most marked in the juxtavesical portion. Here, there was tremendous hypertrophy of the sheath

of Waldeyer, the greatest external diameter measuring 8 mm. There was general muscular hypertrophy seen throughout the ureter and the mucosa was also thickened, the superficial cells being slightly flattened. There was no evidence of any dilatation of the urinary tract. As we have already mentioned, Hofbauer is of the opinion that hypertrophy of the ureteral sheath is the important factor in the production of dilatation in the ureter. However, this observation does not support his views (see Fig. 6, *b*).

It is interesting to speculate why the marked hypertrophic changes occurred in the ureter when associated with the chorionepithelioma. It is known that with the hydatidiform moles and chorionepithelioma there is a great outpouring of prolan in the urine, which produces changes in the vaginal epithelium of the test animal by indirect action through the ovary. This urine when injected into infantile mice causes maturation of the follicles with the production of estrin and a resulting cornification of the vaginal epithelium (estrus); hemorrhage into the enlarged

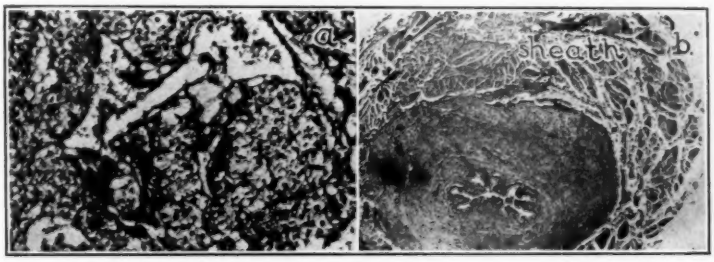

Fig. 6.—*a*, Chorionepithelioma in a man, the primary focus being a teratoma of the testicle (×140).
b, Section of juxtavesical portion of ureter from man with chorionepithelioma, showing hypertrophy of the sheath of Waldeyer even more marked than that seen in pregnancy (×15).

follicles and the formation of corpora lutea of normal appearance; also corpora lutea atretica, characterized by imbedment of the ovum in the lutein tissue (Zondek). It is thought that prolan is free of growth promoting hormone, so in order to explain the hypertrophic changes in the ureter, it would be most logical to deduce that this same indirect action occurred in the patient with the testicular tumor. The prolan elaborated by the trophoblastic tissue of the chorionepithelioma stimulated the testicle with a subsequent outpouring of growth hormone, which in turn produced hypertrophic changes in the ureter.

Having shown that the primary changes in the ureter are hormonal in action, we will now consider the subject of pressure, which is the second etiologic factor in the causation of dilatation.

In early pregnancy, when the uterus is confined to the pelvic bowl, the lower ends of the ureters show lateral displacement, but dilatation of this portion is rarely seen. At the fifteenth to sixteenth week of gestation, the growing uterus, rising out of the pelvis, may now exert

pressure upon the ureter at the pelvic brim. We have shown that a softening process of the ureter takes place with advancing pregnancy. This is of the greatest importance, for without this change, the soft semicystic uterus could not exert sufficient pressure on the unchanged ureter to cause its compression. The right ureter is more affected than the left for several reasons. The left ureter is protected and cushioned by the overlying sigmoid flexure, which also is a causative factor in the production of dextrorotation of the uterus. Baird has called attention to the fact that the right ureter is more exposed than the left, due to its anatomical course, and therefore is more easily compressed. Fig. 7 shows the right ureter crossing the iliac vessels at nearly a right angle; whereas, the left ureter, which is double, runs almost parallel to the

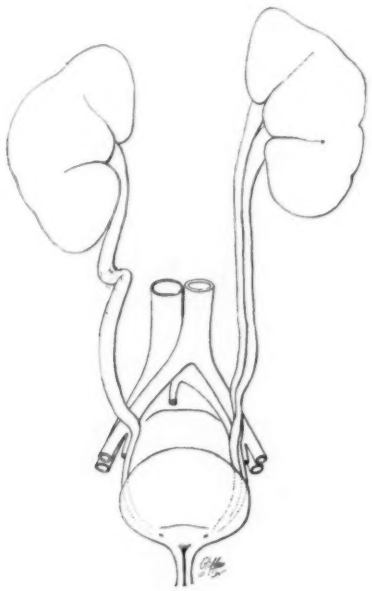

Fig. 7.—Autopsy drawing of urinary tract, patient dying at term. Note right ureter crossing iliac vessels at nearly a right angle, thus making it prominent and more susceptible to pressure than the left ureter, which runs nearly parallel to the iliac vessels.

vessels. This drawing which was made at autopsy, patient dying at term, shows that the dilatation of the abdominal ureter begins at the brim of the pelvis with kinking of its upper portion. The left double ureter is straight and is not dilated; its two portions join at the juxtavesical region and enter the bladder as a single tube with one orifice. The pelvic ureters are not dilated.

One of us (J. M. H.) on several occasions, at operation and autopsy, has observed the markedly compressed ureter at the pelvic brim, produced by the overlying uterus.

We have been able to show definite regression of the ureteral and pelvic dilatations during pregnancy by the use of the indwelling catheter.

It is necessary for the continuous drainage to be maintained for at least forty-eight hours before decrease in capacity is noted. Even with continuous drainage, the decrease in dilatation would not be expected to be so very rapid for the ureter is still atonic and soft, due to the continuous action of estrin.

It has also been demonstrated that large uterine fibroids which fit the pelvis and impinge against the ureters at the pelvic brim produce upper tract dilatations. It is noticed that dilatation changes are not so marked even though some of the tumors have been present for several years. One might expect the dilatations to be more marked due to the greater density and the more prolonged pressure of the fibroma; however, this lack of increased dilatation is probably explained by the nonpregnant ureter being firmer and more compact, and therefore better able to withstand the compression.

Another point to support the theory of pressure is, that in catheterizing the right ureter during the latter part of pregnancy, using a catheter armed with a No. 4 mm. wax bulb, definite obstruction and "hang" are met with at the pelvic brim. When this same procedure is done following delivery, no obstruction or "hang" is encountered, showing that whatever obstruction existed during pregnancy was relieved by the birth of the child.

We are indebted to Dr. Hugh Spencer and his associates, in the Department of Pathology of the University of Maryland, for their cooperation and advice.

We wish to thank Dr. Carl Hartman, of the Department of Embryology of the Carnegie Institution of Washington, for his helpful suggestions.

We also wish to thank Mr. Carl Clarke and Mr. James Dunlop, of the Art Department of the University of Maryland, for these excellent illustrations, and also Miss Evelyn Glidden, of the Art Department of the Johns Hopkins Medical School, for her fine autopsy drawing of the urinary tract.

REFERENCES

Rayer, Pierre: Traite Maladies des Reins **3:** 1841. *Cruveilhier:* Descriptive Anatomy, pp. 585, 586, 1843. *Kretschmer and Heaney:* J. A. M. A. **85:** 406, 1935. *Kretschmer, Heaney, and Ockuly:* J. A. M. A. **101:** 2025, 1933. *Duncan and Seng:* Am. J. Obst. & Gynec. **16:** 557, 1928. *Hofbauer:* Bull. Johns Hopkins Hosp. **42:** 118, 1928; J. Urol. **20:** 413, 1928. *Menees, Miller, and Holly:* Am. J. Roentgenol. **24:** 363, 1930. *Kerr and Mackay:* Edinburgh M. J. **40:** 1933. *Ude, Weum, and Urner:* Am. J. Roentgenol. **31:** 230, 1934. *Lee and Mengert:* J. A. M. A. **102:** 102, 1934. *Baker and Lewis:* J. A. M. A. **104:** 812, 1935. *Bardeleben:* Handbuch der Anatomie des Menschen **7:** Part 1, 1902. *Carson:* J. Urol. **16:** 167, 1926. *Baird, Dugald:* Lancet **2:** 983, 1932. *Mengert:* Am. J. Obst. & Gynec. **27:** 544, 1934. *Carreras, F., Faixat, F., and Figueras, I.:* Rev. españ. de obst. y ginec. **16:** 661, 1931. *Friedl, F.:* Centralbl. f. Gynäk. **57:** 327, 1933. *Mandruzzato, P.:* Ann. di ostet. **53:** 547, 1931. *Jung:* Arch. f. Gynäk. **144:** 578, 1931. *Seng, Magnus:* J. Urol. **21:** 475, 1929.

THE HISTOGENESIS OF CERTAIN OVARIAN TUMORS AND THEIR BIOLOGIC EFFECTS*

SAMUEL H. GEIST, M.D., NEW YORK, N. Y.

(From the Laboratories and Gynecological Service, Mount Sinai Hospital)

THE recent advances in our knowledge of ovarian neoplasms have in great part been based on a better understanding of the embryologic development of the gonad and of the biologic activity of that organ. Unfortunately both of these important concepts in the life history of the ovary are still in a state of flux.

Early in the development of the gonad, the surface epithelium of the *anlage* of the ovary becomes many layered and extends downward into the mesenchyme as solid cell cords. This represents the indifferent gonadal stage. This stage rapidly passes into that of the definitive sex gland. The character and fate of the cell cords from the surface epithelium depend on the type of gonad (male or female) that develops.

In the male the cell cords form the tubular system and possibly the interstitial cells, while in the female they become the undeveloped granulosa and theca interna cells, which later are utilized in the development of the graafian follicle. Fischel, and more recently Schiller, believe that these granulosa cell forerunners and the theca cell forerunners, as well as the interstitial cells of the testis, are derived not from the surface epithelium but from the mesenchyme. The weight of evidence at present, however, favors the coelomic epithelial origin.

In addition to the two-cell types mentioned, there remain in the female gonad remnants of structures that achieve full development only in the male. The structures we identify as cords and tubules in the region of the "rete ovarii." These structures presumably remain quiescent, but may, under proper but as yet undetermined stimulation, develop and functionate in a male direction.

Occasionally gonads are encountered, that are functionally inefficient, the improperly descended gonad (the cryptorchid), the sex glands of the hermaphrodite, or the gonads of hosts that are somatically inferior, as individuals with infantile genitalia and sterility. In these latter cases some of the cells of the original epithelial invasion remain, which not only are functionless, but which do not at any time have the potentiality for developing along male lines as do the rete structures, or along female lines as do the granulosa or theca forerunners.

It is important to keep these embryologic possibilities in mind, for it is this concept that enables us to attempt to classify some tumors histogenetically.

*Presented at a meeting of the New York Obstetrical Society, March 12, 1935.

The ovary has been found to produce at least two definite hormones. One, the estrogenic factor, is apparently developed by the granulosa cells as shown by Frank and the theca cells as proved by Zondek. The second, "progestin," is derived from the corpus luteum as demonstrated by Corner and others. The estrogenic hormone is presumably active in some tumors.

We know that the tumors of various ductless glands give rise to clinical signs and symptoms suggestive of a perverted or exaggerated physiologic activity of the tumor or of the gland itself, as for example, the tumor of the pituitary, thyroid, adrenal, pineal and the gland under discussion, the ovary.

Four tumor types in the ovary may be recognized as distinct entities, and have been classified, because of the belief that one can identify their site of origin, and can also associate with them definite effects which may be recognized clinically.

These groups are: (1) The granulosa cell tumor; (2) the theca interna cell tumor; (3) the arrhenoblastoma, or rete cell tumor; and (4) the dysgerminoma, or indifferent cell tumor.

THE GRANULOSA CELL TUMOR

A group of tumors containing ovalike inclusions were described by Acconci, Emanuel, Amann, Blau, and others. Lippman showed that these inclusions were not ova but cell secretion. Schiminicke pointed out the similarity between the radial arrangement of the cells of these tumors and that of the granulosa cells in the follicles. Many names were suggested by various authors, depending on their interpretation of the origin, or the histologic make-up of these neoplasms. Robert Meyer suggested the persistent primitive granulosa cell balls as the site of origin and the name granulosa cell tumor was then advanced by V. Werdt.

As was mentioned earlier in this paper when discussing the embryology, the surface cell invasion into the underlying mesenchyme probably results in the formation of the active parenchyma of the ovary, and it is from some of these cells, the unused forerunners of the granulosa cells, I believe the granulosa cell tumors arise. The granulosa cell balls have already reached a definite stage of development and would hardly be expected to produce such bizarre tumors as will be described. The undifferentiated forerunner, probably under an as yet unknown stimulus, has a far greater potentiality for variation.

These tumors are usually unilateral. They occur as bilateral tumors in about 10 per cent of the cases (Szathmary). They vary in size from small 6 by 5 mm. tumors (Schiller) (Fig. 1) to masses twice the size of an adult head (Dworzak) (Fig. 2). The surface is encapsulated, usually smooth, with varying sized bosses. As a rule they are soft, mainly solid masses, though cysts may be present, either single or multiple, large or small. The tumor is sessile, but rarely may be pedunculated and thus may undergo torsion.

On section the growth is a medullary, cellular, yellowish tumor. Connective tissue bundles traverse the cut surface irregularly, giving a finely or coarsely lobulated appearance to the cut surface. When cysts are present, their inner wall may be smooth or shaggy, and the contents vary in color and consistency, at times being a thin, yellowish or pinkish fluid, and at others, a thick mucinous or gelatinous grayish white opaque substance.

Hemorrhage may take place into the tumor tissue or even into the cysts, and necrosis of varying extent is not uncommon (Fig. 3).

The histologic picture varies tremendously, though, in the main, three types may be differentiated, the folliculoid, the cylindroid, and the mixed type. The connective tissue arrangement and distribution plays a great rôle in determining the type (Robert Meyer).

Fig. 1.—Small tumor contained in ovary (Goldberger's case). Gross (cylindroid type).

Fig. 2.—Large tumor. Atypical type.

At times in the same tumor all three types of structure may be found and not infrequently only the careful study of many areas will enable one to identify the neoplasm definitely as a granulosa cell tumor.

The folliculoid type, which is the most striking, presents a most unusual picture. (Fig. 4.) The cells are polygonal or round, moderate sized, closely packed, with a central vesicular nucleus, resembling the granulosa cells of the young developing follicle. They form larger and smaller compact cell masses, showing in some instances mitoses, and are surrounded by connective tissue bundles. Fat stains demon-

strate the existence of small amounts of lipoid in these cells, but apparently a greater amount in the connective tissue (Schiller).

In the solid masses one finds small cavities, in places resembling follicles. They are usually round, but may become confluent and give rise to irregularly shaped large-sized cavities. In these cavities, round or oval structures are found, sometimes representing degenerating cells or colloid material or cell secretion. At times a single

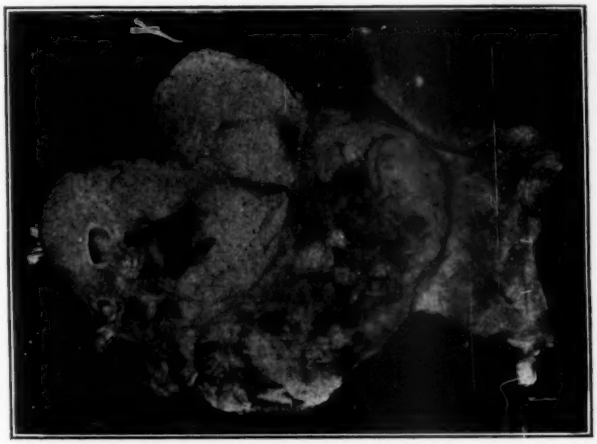

Fig. 3.—Lobulated tumor. Folliculoid type.

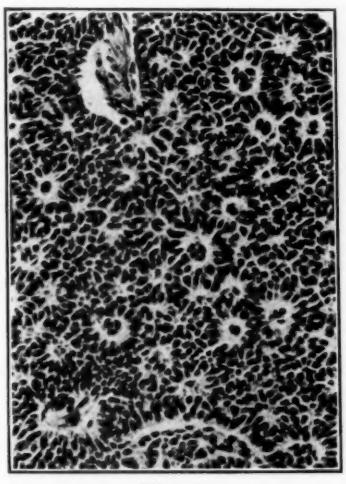

Fig. 4.

Fig. 5.

Fig. 4.—Folliculoid type. Solid cell nests with ovalike structures.
Fig. 5.—Cylindroid type. Solid cell columns separated by connective tissue.

swollen degenerating cell fills the cavity and has been mistaken for an ovum. The cells surrounding the cavity are often radially arranged, and at the periphery of the cell mass where it abuts the connective tissue, the same radial arrangement is present. While this arrangement suggests the follicular origin, it has been shown by Schiminicke to be just an arrangement trait of the tumor cells.

At the periphery and in the substance of the cell masses vacuoles of varying size are found, the so-called Call-Exner bodies, the significance and origin of which are

not known. Similar bodies appear in normal structures, as the granulosa layer and other neoplasms (Schiller). The connective tissue may invade the solid cell masses, subdividing them into small groups. The tumor cells may at times take on a more spindle type, resembling the connective tissue cell.

The cylindroid form is composed of epithelial cells, cuboidal or spindle in type, separated by fine connective tissue bundles. Here, too, spaces are found that may be empty or contain remains of cells or connective tissue. The cell columns may have bizarre shapes, due to the ingrowth and pressure of the connective tissue (Fig. 5). The connective tissue may become hyaline, or remain finely fibrillar. It may even separate individual cells from each other by ingrowths of fine fibers or so demarcate the cell column as to give a picture of wavy pattern, the so-called moiré silk type.

One often finds a combination of the folliculoid and cylindromatous types, and not infrequently a sarcomatous form, in which it is necessary to make careful studies to identify the true nature of the growth. This latter type is composed of spindle (Fig. 6) or polymorphous cells that intermix with no definite arrangement. Here and there one finds more epithelial-like cell groups, and some definite areas that are typically granulosa cell in type. The cells are separated into large groups by con-

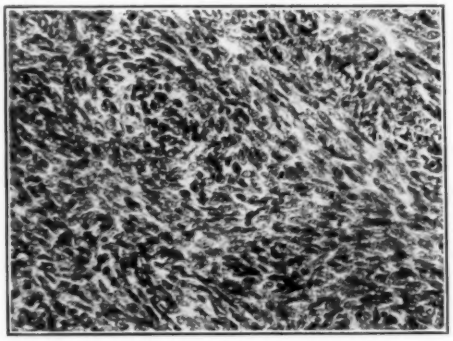

Fig. 6.—Sarcoma-like tumor.

nective tissue bundles containing vessels, and this lobular structure may even be noted grossly. In some areas tubular structures are found, and rosettes of tumor cells may occur to further complicate the picture. At times adenomatous areas are found, or small round tubules with rather slender high cuboidal epithelium and no evidence of a follicular type.

Primarily the tumors are solid but they may undergo degenerative changes due to circulatory disturbances. Areas of hemorrhage, necrosis, and cyst formation are not infrequently encountered. The cysts, both large and small, are the results of degeneration. Burg reported a case with 5 liters of fluid and a small solid portion only. The possibility of the cell secretion forming small spaces and later from pressure causing cell death must be kept in mind, for often the remains of cells, nuclear fragments and granular débris are found in these small follicle-like spaces. The radical arrangement of the border cells suggests a follicle, but this tendency is common in any growth process where degeneration takes place. The lining of the cysts when present is usually a low epithelium.

It is possible that the cell secretion contains the hormone which we now know is present in these tumors, and which, we believe, acts on the host to produce the distinctive clinical picture which so commonly is associated with granulosa cell tumors. Lipoid is present in these tumors. It is found in the cells, but more often and in

larger amounts in the connective tissue (Schiller). This is in contrast to the theca cell tumors as will be mentioned later, where the lipoid is found almost exclusively in the cellular islands.

R. Meyer, Neumann, Klaften, Siebke, Suschania, and Salmon found an estrogenic hormone in these tumors, but not in large amounts. Pahl, in a child of nine with a granulosa cell tumor, reports a positive Aschheim-Zondek test.

The granulosa cell tumors may occur at any age though the fourth and fifth decade is the most common. Klaften states that they occur before puberty in 8.9 per cent, during sexual activity in 48.7 per cent, and at or after the menopause in 42.5 per cent. He reported the case of a patient nine years of age with precocious puberty. After removal of the tumor the symptoms regressed. Novak reported cases at three, five, and six years, respectively, all with pubertas precox. Other authors also have reported cases in children (Szathmàry), all with atypical bleeding, with pubic and axillary hair, and adult-sized pelvic organs. In one case, a child, reported by Meyer, colostrum was present in the breasts. Bland and Goldstein detail a case with a positive estrin finding in the urine two days before operation, and negative seven days postoperative. This patient was seven years old with precocious sexual development.

The tumor may occur in very old women between seventy and eighty as reported by Schroeder, Isbruck, Neumann, Schiller, Schiffman and others, with or without atypical bleeding, but usually with a well-preserved uterus and hyperplastic endometrium.

The most striking distinctive symptom is irregular uterine bleeding, sometimes of long duration, and occasionally preceded by short periods of amenorrhea, or, as in a case of Plate, followed by amenorrhea. We recently had a case in a woman of thirty-six with a three-year period of amenorrhea, a resting endometrium and a small endometrial polyp associated with an atypical granulosa cell tumor with abundant estrogenic hormone in the tumor tissue (Salmon).

The uterus is usually soft, hyperemic and enlarged. The myometrium is hypertrophied and the endometrium is hyperplastic. Adenomatous polyps of the uterus are not infrequently encountered.

Habbe reports four cases in the climacteric with endometrial hyperplasia, but without a history of bleeding, while Schroeder mentions a case in a woman thirty-six, with menstrual irregularities and an atrophic mucosa.

Klaften has found glycogen in the hyperplastic mucosa when the hyperplasia was the result of tumor activity even in the climacteric.

Tietze has reported hypertrophy of the tubal epithelium.

The breasts are not infrequently enlarged, a fact that one attempts also to correlate with the tumor activity. This enlargement regresses with the removal of the tumor. Klaften has reported hirsutism which has not regressed with the ablation of the growth and is probably not related to the tumor. Bergstrand reports six cases with hirsutism. Klaften has reported an increase in the basal metabolic rate in one instance as high as plus 24, which returned to normal following removal of the neoplasm. Ascites is not common, though Szathmàry reports it in 10 per cent of the cases. Adhesions occur only late in the disease.

The tumors often present the histologic picture of malignant neoplasms, with cell atypism and mitoses, and at times infiltration. Schiller divides them into malignant and nonmalignant, stating however that the division is really clinical and not histologic.

They rarely recur and if they do, the recurrence is usually local. The removal of the second tumor may be followed by a permanent cure. Szathmàry reports 10 per cent of local recurrence, and 15 per cent in the opposite ovary.

The benign cases are usually unilateral and Schiller states that when unilateral they are practically always benign. The involvement of the second ovary may be

metastatic, secondary invasion or primary involvement. Schiller has suggested the term granulosa cell tumor for the benign, and granulosa cell carcinoma for the malignant.

Metastases are rare but occur not only locally, or in the other ovary, but also in the abdominal viscera and retroperitoneal lymph nodes. Soltman reports metastases in the bones; and Maresch, also. Granulosa cell tumors may arise in the retroperitoneal ovarian segments, and Stoltz states that in 69 per cent of supernumerary ovarian segments some type of tumor has been present in them.

Granulosa cell tumors when benign are easily treated by operative removal and the patient may and does remain well and physiologically normal. Pregnancy even has followed. In the malignant type, when a recurrence develops it may be benign (Schiller) or malignant in type. With the appearance of recurrence or metastasis, the typical clinical signs may reappear, to regress on subsequent removal of the growth. The prognosis is good. In 7.5 per cent of the cases, however (Klaften), they were inoperable.

A large number of patients with malignant cases have been treated with postoperative radiotherapy (Klaften, Plate, Schiffman, Habbe, Dworzak, Schulze) with good result.

These tumors have been investigated for their hormone content. As before mentioned, while it has been found by transplantation experiments, the estrogenic hormone has been isolated also by tumor extraction. In one of our cases Dr. Salmon has obtained one mouse unit per gram of tumor. Dworzak and Podleschka report a case with 50 m. u. per liter of urine in the intermenstruum. This, however, is not an unusual amount.

With the removal of the tumor the bleeding, breast enlargement, and uterine mucosal hyperplasia regress. With the appearance of a recurrence these symptoms again make their appearance, indicating the part played by the tumor tissue. These findings suggest that the clinical symptoms are due, at least in part, to the activity of the hormone.

It is evident that here we have a distinctive tumor, both histologically and clinically, whose cells produce a hormone that affects the normal physiology of the host, i.e., a tumor that has a genetic, morphologic and biologic resemblance to granulosa cells.

THECA CELL TUMORS

In 1932 Löffler and Priesel described a group of tumors, six in number, which because of their distinctive gross, histologic and clinical characteristics, they believed were derived from the theca cells, forerunners in the ovarian parenchyma. In 1934 they reported four additional cases.

The parenchymal cells, both granulosa and theca interna, have definite common characteristics: both store or form lipoid and both produce or store an estrogenic hormone. Zondek showed that the theca interna cells contain an estrogenic hormone, usually in greater amount than in the granulosa cells. In addition both cell types stimulate the formation of connective tissue, which has a tendency to become hyalinized, though this is more marked in the theca cells. In addition, these latter cells may even produce fine connective tissue fibrils.

The theca cell tumors have all these characteristics coupled with a striking morphologic pattern, and nowhere showing areas suggestive of granulosa cell tumor, thus leading us to believe that they form a separate and distinct group. In addition, the distribution of the lipoid in the theca cell tumors differs from that in the granulosa cell tumors. In the latter the lipoid is found mainly in the connective tissue bundles (Schiller), while in the theca tumor the lipoid is found almost entirely in the cell islands, and only as small droplets in the connective tissue or at its periphery.

Grossly the theca cell tumors are distinctly different from the granulosa cell growth. Furthermore, the consistency and appearance in many instances is that of a fibroma, whereas the granulosa cell tumor is a cellular, softer tumor. The hormone content also of the theca tumor in the one case examined was far greater in amount than that as yet reported in the granulosa cell tumor. Finally in all but two of the sixteen cases now recorded they occurred in women at or past the menopause.

Löffler and Priesel have reported in two publications ten cases, Melnik and Kantor have two additional cases, and we have had four cases of our own. (These latter cases will be reported in detail elsewhere.)

Grossly these tumors appear as hard, somewhat nodular tumors, which may reach the size of a child's head (Fig. 7). In one of our own cases it was represented by a large twisted cystic mass, the wall of which measured 2 cm. in thickness and was of a bright yellow color. The surface is smooth. It is hard except in the cystic type and suggests a fibroma grossly.

Fig. 7.—Fibroma-like tumor with small cellular areas (theca).

On section it has a striking appearance. The surface has a yellowish white color. On close inspection the tumor is seen to be composed of varying sized yellow islands separated by fine or coarser hyalinized connective tissue bundles (Fig. 7). Small hemorrhages may be present, and at times, cysts vary in size from pinhead to walnut. These may coalesce and form larger ones as in one of our cases. These cysts are degenerative in origin.

On the other hand, the cut section may present broad white glassy areas of connective tissue, with here and there, in these areas, tiny pinhead-sized islands of yellow color, and in addition, large isolated nodules of yellow tissue surrounded by the hyaline fibrous tissue (Fig. 8). Few blood vessels are present, except near the connective tissue capsule at the surface, and at the periphery of the fatty islands.

Histologically the tumors are very distinctive in structure. The yellow areas are composed of plump spindle cells or polygonal cells with central or at times excentric nuclei, dark staining and rich in chromatin. The cell protoplasm is vacuolated and contains fat (Fig. 9). The fat globules may also be present in the interstitial tissue to some extent, but only where cells still are present, and then usually as much smaller globules than in the cellular islands (Fig. 10). The epithelioid cells seem to have a tendency to be more numerous about the vessels.

The connective tissue bundles are hyaline to a great extent, and often large hyaline plaques are present in the midst of a cellular island (Fig. 11) with fine fibers extending out radially and surrounding the individual cells or seeming to enter them.

Fig. 8.

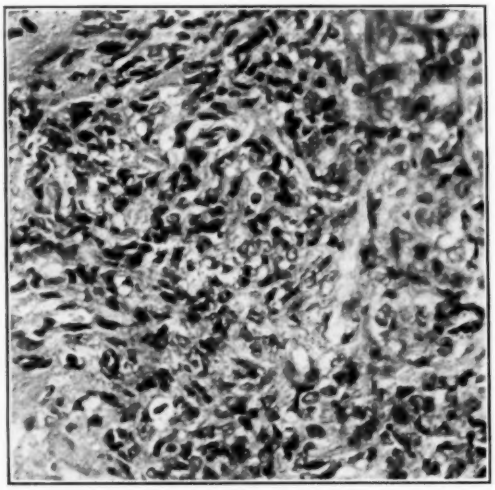

Fig. 9.

Fig. 8.—Hyaline type with well-demarcated cellular islands.
Fig. 9.—Cellular areas with vacuoles.

Fig. 10.

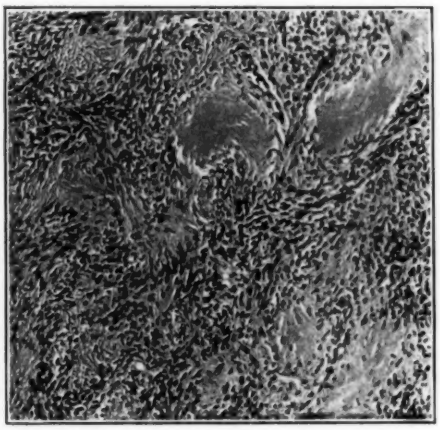

Fig. 11.

Fig. 10.—Fat in cellular areas, little in connective tissue areas.
Fig. 11.—Hyaline plaques with fibers radiating into cellular areas.

The fibrous tissue bundles vary in size, density, and structure. They may be very fine, composed of but a few fibrils, or so massive as to represent the greater part of the tumor as in one of our cases. They may be composed of few connective tissue bundles or large masses of hyaline tissue, and they may show many or few connective tissue cells with isolated, large, fat-containing cells in the meshes

of tissue. At the periphery of the hyaline plaques some fat droplets are present. Pigment granules, probably lipochrome, are found in some of the epithelioid cells, but mainly in the capillary endothelium. The cystic tumor previously mentioned had a 2 cm. thick wall composed of elements as above described.

The cysts when present may be smooth walled or shaggy. They contain a yellowish clear or turbid fluid and show no definite epithelial lining. Rarely a flattened endothelial-like lining is present in scattered areas.

Chemical analysis of the tumor shows it to contain a not unusual amount of lipoid, but a relatively high content of cholesterin and cholesterin ester. The polaroscopic examination demonstrates that most of the fat is double refractile, and is in the cell islands.*

The extraction of the tumor tissue also demonstrated that it contained a large amount of estrogenic hormone per gram. This fact helps to understand and explain some of the clinical symptoms and signs. In one case, already submitted for publication, in association with Spielman, we were able to demonstrate more than a mouse unit of estrogenic hormone per gram of tumor tissue.

The tumor is unilateral. In all the cases reported (sixteen) only two occurred in women before the menopause, one of Löffler and Priesel, at eighteen years, and one of ours, at twenty-one years of age.

Aside from the symptoms of any pelvic neoplasm of size, these tumors have certain definite and clear-cut symptoms. The most striking is atypical bleeding, naturally postmenopausal, as this is the common age of occurrence. In our patient, of twenty-one years of age, there had been a history of bleeding for one year, and then a short period of amenorrhea. In the case of Löffler and Priesel, at eighteen years, a similar history was obtained. In addition in our case the patient noted an enlargement of the breasts.

The uterus is usually enlarged and soft, and in those cases where the endometrium was obtained, it was hyperplastic. After the removal of the tumor all the symptoms regress.

While Löffler and Priesel report a case as malignant, all the other patients thus far reported have apparently been cured by operation. In all probability a unilateral oophorectomy is all that is indicated.

Here again is a distinct tumor type, histologically, chemically, and biologically, suggesting the undeveloped theca cell as its source of origin.

ARRHENOBLASTOMA

Virilism or masculinization in a previously normal female is a characteristic of a definite tumor type that is found in the ovary. At times somewhat similar pictures can be produced by tumors of the adrenal. Hirsutism alone has been described associated with granulosa cell tumors and even in women with no demonstrable lesion (Spielman).

Robert Meyer has attempted to group two types of ovarian growth under the common term arrhenoblastoma. He includes the so-called adenoma testiculare ovarii, first described by Pick, which he terms the typical form, and an atypical form, the true arrhenoblastoma, believing that both neoplasms have a common histogenesis.

The question raised by Pick is one of origin. He was of the opinion that the tubular adenoma, first described by him, arose in the testicular portion of an ovotestis. R. Meyer, however, believes that these adenomas, as well as the more atypical growths, arise from the embryonal vestigial remnants of the medullary cords

*This study was carried on in collaboration with Dr. Rosenthal of the clinical laboratory, Mount Sinai Hospital.

and rete tubules of the ovary. He points out the fact that in the adenoma tubulare there are no evidences of hermaphrodism as one might be led to expect in an individual harboring an ovotestis.

The typical adenomas only rarely cause masculinization, while the atypical usually do. Meyer believes that this variation in physiologic effect need not imply a different origin, but merely a difference in the degree of development of the anlage. The masculinizing form of the tumor arises from cells that still retain the male hormonal influence which may be activated by some stimulus.

In fact, though the typical adenoma described by Pick and the atypical one of Meyer seem not at all related in morphologic appearance, in an intermediate group of six cases, five of Meyer's and one of Popoff's, Meyer showed various stages of transition from the tubular adenoma to the atypical form. In all the cases masculinization of the host appeared in varying degrees. This manifests itself in amenorrhea, masculine voice type, at times masculine carriage, and facial appearance, or hirsutism confined to the arms and legs and face.

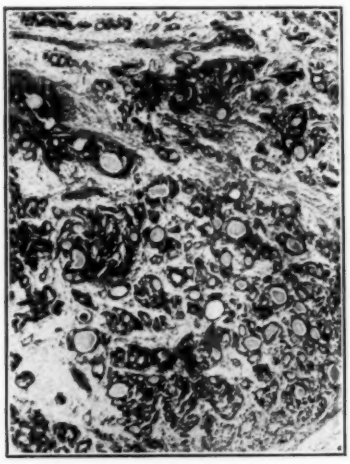

Fig. 12.

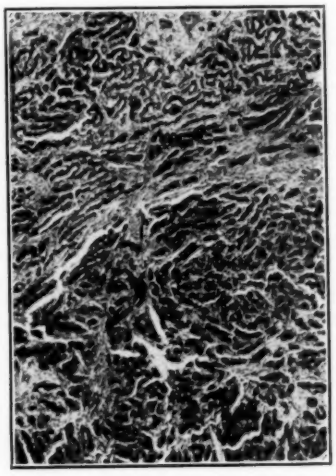

Fig. 13.

Fig. 12.—Intermediate type, regular and irregular tubules.

Fig. 13.—Intermediate type, solid cords and irregular tubules. (Same case as Fig. 12.)

The typical adenoma testiculare ovarii is usually a small tumor, firm, encapsulated, or embedded in the ovarian structure, and composed of regular tubules with a small circular lumen, lined by a layer of cuboidal cells, supported in a dense connective tissue. In one case reported by H. O. Neumann, the presence of cells resembling the interstitial cells of the testicle made the resemblance to the true testicular adenoma of the male gonad very striking.

The intermediate group of atypical tumors are larger growths than the typical ones, reaching the size of an adult head, and are unilateral. They have a lobulated surface, are encapsulated, smooth, and may infiltrate the surrounding structures. On section they are soft, medullary-like yellowish growths with a marked tendency to undergo regressive changes. Hemorrhage, necrosis, and liquefaction are present, and in some instances true cysts with an epithelial lining may be present. Some of these tumors may simulate cysts, and their true identity may be extremely difficult to establish. The tubules are irregular, their lumina varying in size and contour (Figs. 12 and 13). Some of the epithelial cells undergo fatty degeneration.

As the more atypical group is approached the tumor pattern (Fig. 14) varies markedly from the pure tubular or partly tubular and partly cellular-like growth of the intermediate type. In the main the tumor is solid with a few atypical tortuous tubular areas, or areas of convoluted solid cords of cells (Fig. 15). These cell cords can at times be recognized as composed of cells resembling the more sarcomatous appearing elements that may form the bulk of the growth. The stroma may become sarcomatous (Strassman). There are evidences of cyst formation with epithelial lining and even papillae (Robert Meyer), and Beuttner and Meyer have described mucinous epithelium.

As to the histogenesis, the probability of both tumor types, the typical and atypical, arising from the embryonal remains of testicular structures in the rete ovarii is most likely. However, the possibility of their origin, especially of the true adenomas, from a congenital ovotestis cannot be disproved.

The typical testicular type has no incretory function. Only in those tumors whose cells deviate from the normal do we have the presumed production of a masculinizing hormone.

Fig. 14.

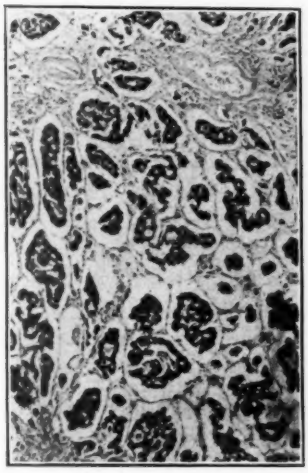

Fig. 15.

Fig. 14.—Hemorrhagic tumor (Spielman's case).
Fig. 15.—Atypical type with solid cords and tubules (Spielman's case).

Clinically these tumors affect the individual by, as before mentioned, changing her from a typical female to a masculine type. The menses cease, the breasts atrophy. The pelvic organs both external and internal likewise atrophy, except the clitoris, which may enlarge. There is a marked change in the facial appearance; it takes on a masculine appearance. Excessive hair development takes place on the face, especially on the upper lip, the chin, and the cheeks. Hair also appears on the chest and the extremities. The voice changes from the high-pitched feminine note to the deep low-toned male type, or may be cracked as in puberty. The gait is more that of the male stride than the mincing step of the female. The libido is adversely affected, and the normal interest in the opposite sex may disappear.

These symptoms with the removal of the tumor may subside. Cases are reported where pregnancy has supervened after the removal of the tumor, terminated by a

normal labor and a normal child (Sedlaczek, Mathias, Neumann and Popoff). With the appearance of a recurrence the typical masculinizing syndrome may again be present.

While these tumors may present the histologic signs of malignancy, many of the patients have been successfully operated upon and permanently cured. Strassman reported thirteen cases, and all but one were malignant.

This tumor group is of distinctive histologic appearance and suggests the probability that the cells of the rete ovarii are the source of the neoplasm. In addition they present a typical clinical syndrome and probably contain a hormone that stimulates the development of the male characteristics, or negates the female influence, to permit some basic male principle to dominate.

DYSGERMINOMA

An unusual ovarian neoplasm is one previously called seminoma, by Chenat and Bender, because of its resemblance to the typical seminoma found in cryptorchids. Pick called it epithelioma-chorioectodermale. This type of growth occurs usually in a gonad that is functionally inefficient and has been described not only in the ovary and testis but also in ovotestis (Unger, Pick, and Polano). In addition, the host is not infrequently hermaphroditic as has been pointed out both by R. Meyer and H. O. Neumann.

The tumors may involve only one gonad or both. When one gonad is involved the other may be absent or so atypical that the identification of its type may be impossible. When both gonads are involved, they may be so completely replaced by tumor that it is impossible to determine the sex of the gonad. It must also be stated that in some instances the tumor may be present in a perfectly normal individual with a normal gonad on the other side, as in two of our cases.

E. Fauvet reports 27 cases from the literature in male or female hermaphrodites, 2 in true hermaphrodites, and 35 in normal women.

H. Kleine reported 7 cases, all in asthenic young women fifteen to twenty years of age. In one case the patient subsequently had one child, in another case two children.

We have had 3 cases, 2 in children twelve and fourteen years old, and one fifteen years old. The latter patient had menstruated normally for two years before operation. In the small fragment of ovarian tissue attached to a small mass of tumor from the second ovary, normal follicles, stroma, and corpora albicantia were present.

The tumors may reach the size of an adult head (Fig. 16). The surface has a capsule which may be intact or perforated by the growth, which then extends into adjacent structures. The surface may be smooth or bossed. Its consistency is elastic, though in places due to the breaking down of the growth and the formation of cysts it may be almost fluctuant.

On section it has a grayish yellow appearance, cellular, medullary, almost brain-like. Areas of necrosis, hemorrhagic and cyst formation may be found. Extension into the uterus and other gonad may be present, as in two of our cases.

Histologically the picture aside from the degenerative areas is strikingly uniform. The mass is composed of large round cells with a light granular cytoplasm and a round central nucleus. The cells are loosely arranged in columns and larger and smaller islands, separated by connective tissue strands. The connective tissue varies in amount, being scant in some places and better developed in others. In these strands, blood vessels are present, and numerous collections of small lymphocytes (Figs. 17 and 18). This latter characteristic is most striking.

The growth is most commonly found in children and young adults, usually individuals whose gonads are not functioning normally, so that as before mentioned,

hermaphroditic persons are frequently encountered. In addition, if the host is a typical female, the genitalia, both internal and external, may be infantile in type. It may occur in older women (Neumann), and Gross had a patient who had borne a child. It is usually unilateral, becoming bilateral only late in the disease.

The tumor apparently has no incretory function and thus does not affect the individual either in a female direction as do the granulosa or theca cell tumors, or

Fig. 16.—Gross lobulated tumor.

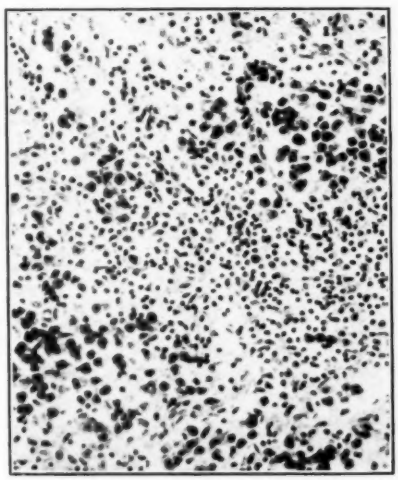

Fig. 17.

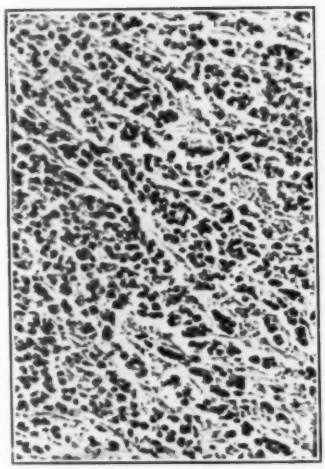

Fig. 18.

Fig. 17.—Cell cords and columns with scant loose connective tissue and lymphocytic infiltration.

Fig. 18.—Cell cords of large round cells with lymphocytic involvement.

in a masculine direction as does the arrhenoblastoma. These tumors apparently arise from cells probably of germinal epithelial origin which have lost their potentiality to become differentiated into either male or female cell types. In other words the cell of origin is a neutral cell, which can be classed as dysgerminal. It is from this term that R. Meyer suggested the name dysgerminoma.

Clinically the tumor causes no definite symptoms other than those of any pelvic growth. It is again to be stressed that the physical make-up of the host, either a pseudohermaphrodite or a young patient with atrophic genitalia, suggests the diagnosis.

The tumors are malignant, and unilateral removal may result in early recurrence or metastases in the retroperitoneal lymph nodes, the other ovary, peritoneum, pleura, or omentum. We have had occasion to operate upon several of these patients, and have found that operation followed by radiotherapy offers an excellent chance of permanent cure.

Robert Meyer has had patients who have survived four, six, and eight years, respectively.

To recapitulate, we have described four groups of tumors.

1. The granulosa cell tumor arising from unused granulosa cell forerunners in the ovary. These tumors have a definite incretory function: they store or produce the estrogenic hormone. They affect the host by exaggerating certain aspects of the female physiology. They cause an increase in amount and frequency of the uterine bleeding. They stimulate the growth of the breasts and uterus, and cause a hyperplasia of the endometrium, in other words an overfeminization of the individual.

2. The theca cell tumor represents a group arising from the forerunners of the theca interna cells. These tumors in their biologic aspect are similar to the granulosa cell tumor, but are commonly found in the postmenopausal period, and differ so in other aspects from the granulosa cell tumors as to warrant their being regarded as distinct from this group.

3. The arrhenoblastoma is a neoplasm which arises from male-directed elements which have remained quiescent in the ovary, or as Pick believes from the male portion of an ovotestis. These growths presumably contain a male sex hormone, though this as yet has not been proved. They affect the host by causing a defeminization or as some express it a masculinization with the development of male hair type, male gait, voice, and larynx. The loss of the female breast contour, the loss of menstruation, and the atrophy of the genitalia also occur.

4. The dysgerminoma arises from neuter cells of germinal epithelial origin, i.e., dysgerminal elements. It has no incretory function and no pathologic physiologic effect on the host, but is found often in individuals with defective gonads and atypical somatic development.

Investigation of tumors of the ovary with these points in mind may help us to understand better the physiology of the normal gonads and enable us to classify ovarian neoplasms more definitely.*

100 EAST SEVENTY-FOURTH STREET

*Note: For lack of space the extensive bibliography cannot be included but may be found in the author's reprints.

THE TOXEMIAS OF LATE PREGNANCY*

WILLIAM A. THOMAS, M.D., EDWARD D. ALLEN, M.D.,
CARL P. BAUER, M.D., AND M. R. FREELAND, PH.D., CHICAGO, ILL.
(From Rush Medical College and Presbyterian Hospital)

THE studies here reported arose from the application of the principles and knowledge utilized in our nephritic studies to the problems encountered in the toxemias of late pregnancy.

All patients, private and in the prenatal clinics, exhibiting any deviation from normal, such as hypertension, albuminuria, headache, visual disturbances, or edema, were hospitalized and subjected to intensive study, and the studies repeated as frequently as the condition warranted.

We have selected those tests which most accurately represent the various changes found in the toxemias and applied these tests to ascertain more definitely,

1. In which cases pregnancy must be terminated.
2. Which cases may be safely carried on with the object of obtaining a viable child.
3. In what form the toxemia will manifest itself should pregnancy continue.
4. The degree of permanent damage suffered by the mother in the cases allowed to progress.
5. The effect of toxemias on infant mortality.
6. To distinguish between toxemia, and nephritis occurring as an entity during the course of pregnancy.
7. In particular to evaluate the efficacy of the procedures used in preventing and combating this condition.

It becomes increasingly clear that the toxemia of pregnancy is not a definite entity, following a fixed course and governed by predicable rules. For example, it has been extensively taught that toxemia occurs most frequently in the first pregnancy and that one attack usually confers immunity. Our experience shows this to be far from the case. Many of the severe cases occur after several normal pregnancies; in others, successive pregnancies exhibited earlier and more severe manifestations.

The course of the disease may vary to any extent in severity and clinical manifestation, depending upon the tissues bearing the brunt of the damage. These causes may be toxic infections or metabolic. There is no single test which accurately represents this damage, since

*Read at a meeting of the Chicago Gynecological Society, May 17, 1935.
This work was carried on with a grant from the Anna Louise Raymond Fund.

one will give entirely normal results while others show evidence of extreme disability. In both these conditions, understanding comes from painstaking analysis of all findings, clinical and laboratory, and a correct correlation of the tests and their significance.

Our studies indicate that in these toxemias, certain tissues or tissue aggregates are particularly susceptible to injury; that the degree of involvement of each is distinctly independent of all others; and that certain tests are definitely valuable in ascertaining the functional state of each of these systems. To be more concrete, toxemias manifest themselves in a great proportion of cases by involving one or more of the following tissue aggregates, each with its own peculiar train of symptoms dominating.

I. *Vascular-renal:* resembles nephritis; blood in urine, albumin, hypertension, retinal changes, spasm and exudate if severe.

II. *Central nervous system:* eclamptic; headache, nausea and vomiting, convulsions.

This type possibly involves posterior pituitary with increase of pressor and antidiuretic principles. This may occur with or without hypertension, possibly dependent upon posterior pituitary involvement. Hypertension of this type is distinctly different from pure vascular or nephritic type and response to treatment differs.

III. *Tissue type:* resembles nephrosis; general involvement of nonspecialized tissues, edema and albuminuria, frequently without hypertension of headache.

IV. *Liver:* prostration; nausea and vomiting; convulsions, shock (collapse and death), with hypotension; either antepartum or postpartum.

Obviously, these four systems may be involved to approximately equal degree or there may be any degree of individual variation. Consequently, a test which accurately represents the grade of incapacity of one group is in no sense an index of damage elsewhere. It becomes necessary to take definite issue with those who advocate any set test or tests as representing the true state of these patients. One group of investigators adheres absolutely to the urea clearance test, setting arbitrary limits below which all patients are in a hazardous condition and above which there is little cause for concern. From another source comes a fixed system of blood pressure readings, and cases are rated according to the strata into which their systolic pressures delegate them. Any such complacent attitude gives either a false sense of security or an unjustifiably grave outlook, for reasons already stated. Unless one is familiar with and competent to judge the interpretation and significance of any or all of these methods of precision, he will do better to proceed on the clinical basis, with due regard to all the manifestations. The errors liable to be encountered in this latter method will be referred to later (circulatory asthenia, etc.).

For example, there very recently came into the hospital a multipara at full term with a history of 6 normal pregnancies. On admission her pressure was 260/140;

albumin +++; she was almost totally blind and retinal examination revealed extensive exudates with high degree of retinal vessel involvement. The routine tests were hurriedly made and labor induced. Two urea clearance tests of 140 per cent and 110 per cent (average 125 per cent) and liver function of normal indicate the fallacy of relying upon the former in such conditions. Repeatedly, patients with urea clearances far below accepted limits of normal have been successfully carried to term, while others with entirely satisfactory urea clearance tests have progressed to such a grave state by clinical and other standards that there remained no choice but to terminate the pregnancy.

Another group of cases has been of great interest. These women, seen in the clinic, with large amounts of albumin in the urine, enter the hospital at once. On the following morning the urine is consistently free of albumin while in bed. Urea clearance figures are high, often 200 per cent or more, and all other tests are normal. These women are definitely a type of circulatory insufficiency. Their hearts are always normal, never decompensated, but often small for their size (for they are usually obese), but the outstanding feature is probably the fact that their arteries and systemic circulatory apparatus are inadequate for their bulk, particularly under the increased load of pregnancy and normal activity. Undoubtedly many such cases are considered as impending toxemias and aborted. Such cases have been repeatedly hospitalized for tests and, following delivery, apparently have normal findings. Thus, albuminuria, even in extreme quantities, may not be of specific significance in pregnancy.

At this point it seems reasonable to emphasize certain facts that are evident to students of nephritis and to call attention to a more abstract but significant theory. This theory removes from the realm of renal insufficiency definite clinical phenomena and places them in the extrarenal or tissue field. In the first place, it is generally evident that neither the external phase of water balance, represented by excretion, anuria, diuresis, and their variations, nor the internal phase, chiefly edema and dehydration, are to any great degree dependent upon ability of the kidneys to excrete water, but parallel much more closely the state of protoplasm, represented by cellular activity, electrolyte distribution, metabolic disturbances, and activities of various glands of internal secretion.

Second, it is becoming increasingly evident that the concentration of electrolytes and metabolites in the blood, that is, blood chemistry readings, is in no respect a function of renal capacity, but represents the level at which osmotic equilibrium occurs between tissues and blood. This means that we have no direct concern with the levels of blood chemistry, except so far as they accurately represent the tissue and cellular concentrations, and that whatever clinical symptoms occur synchronously with elevated blood chemistry findings are due to the tissue concentration of these metabolites, rather than to their

accumulation in the blood. To make the analogy complete, failure of the kidneys to excrete water is not due to renal inability, but to primary claim of tissue thirst on the free blood water. Diuresis will occur, without renal change, whenever the state of tissue metabolism so improves that tissue-bound water is released and this water returning to the circulation is again available for renal excretion.

Similarly, when, due to disturbances of cellular metabolism, such changes occur so as to result in tissue accumulation of electrolytes and metabolites, there must result an osmotic equilibrium between blood and tissues before there are excess substances for renal excretion. As long as the tissue pathology results in this excess content, so long will the blood figures remain elevated. Should any improvement in this tissue state decrease their abnormal content, releasing into the blood the accumulated metabolites, the kidneys will in practically all states excrete this excess, so that the blood figures will reflect the improved tissue state.

Let us visualize two men: one entirely normal with urea nitrogen of 10 mg. and nonprotein nitrogen of 25 mg. per 100 c.c.; the other a chronic but stabilized case of Bright's disease, with urea nitrogen of 40 mg. and nonprotein nitrogen of 100 mg. per 100 c.c. For one year, each is given an identical diet with 100 gm. of protein daily, following which blood chemistry findings are identical with those of a year before. Have the kidneys of one or the other done more work in excreting end products of protein metabolism? The answer is obviously that each has done the same. Furthermore, had the nephritic patient had a markedly lower protein allowance, his final blood chemistry levels would not have been modified, and clinical experience indicates that had the level of protein feeding been increased there would have been no additional accumulation in the blood.

Two conclusions may be drawn from these facts: (1) that the level of blood chemistry determinations is not a function of renal activity, but of the state of tissue integrity; and (2) that the high urea clearance figures in the women with circulatory insufficiency are due, not to any extraordinary capacity of kidneys, but to the release into the circulation, available for excretion, of urea that had accumulated in the tissues during a period in which these tissues were in a subactive state.

These facts naturally throw some doubt upon the validity of the conception of the urea clearance test as a definite function of glomerular activity or capacity and suggest that it may indicate more definitely the state of tissue activity. In any event, this and other accumulating evidence is sufficient to justify its rejection as the sine qua non of toxemias.

Furthermore, the problem of blood sugar raises significant points. Episodes of two types may occur: transient glycosuria associated with elevation of blood sugar, especially in the earlier months of pregnancy; and persistent hypoglycemia in the later stages, particularly in the toxemias. Fundamentally, these fluctuations have been attributed to pancreatic disturbances. Recent investigations (see Collip, J. A. M. A., March 9, 1935) indicate a close relationship between activity of the anterior pituitary and the pancreas. Since abnormal activity of the anterior pituitary is increasingly evident in toxemias of pregnancy, some correlation between that function and the blood sugar may be discovered. Furthermore, the liver as the principal organ in removing glucose from the blood, synthesizing it as glycogen and releasing it upon appropriate stimuli, being frequently the seat of extensive damage in these conditions, may itself be responsible for the lowered blood sugar so constantly found. These surmises are not only theoretical, but may point the way to a clearer understanding of the basic derangements causing toxemias of pregnancy.

With these considerations as a background, a brief summary of our conclusions is given:

Blood chemistry levels, with the exception of blood sugars, have been of no importance in these states, except to designate as nephritic those cases which clearly fall into that class either as preexisting Bright's disease or as the latent condition aggravated by the metabolic load of pregnancy. Even the type of toxemia previously designated as nephritic does not show any degree of accumulation of metabolites. (This is in accord with the conclusions of numerous investigators.)

Urea clearance test, when considered as a relative index, possibly of renal damage and probably of tissue disturbance, is a valuable guide. There is no critical level, and its value lies in repeated tests to determine its trend. The condition may be most grave in the presence of high urea clearance, and favorable even when reduced to quite low levels. The progressive decrease of clearance is regarded as ominous.

Liver function: Numerous satisfactory liver function tests are reported from various sources, with few exceptions, however, related to toxemias of this type.

Bilirubin clearance and bromsulphalein are highly regarded in some quarters.

In our hands the galactose tolerance test is of no value whatsoever, since it is very insensitive and extreme liver damage (both clinical and by other tests) occurs before the galactose test gives any indication of damage.

After numerous trials, we found the Rose-Bengal test most accurately to represent the functions in which we are interested. It is simple, inexpensive, easily read either by spectroscope or colorimeter, and gives early and accurate evidence of the liver type of damage

which leads to one of the severe and serious types of toxemic manifestations, namely, convulsions, shock, and collapse.

Skin absorption time, as advocated by McClure and Aldrich, is of the same significance as in Bright's disease, an evidence of edema, either impending or decreasing, and represents accurately changes in tissue thirst. In extensive edema, it indicates whether or not therapeutic measures are succeeding, and absorption time shorter than normal, in the absence of definite edema, warns of tissue damage and probability of ensuing edema.

Concentration tests and modified Mosenthal are of the same significance as in nephritis. They do not indicate integrity or impairment of renal function, but hydrophilic state of tissues.

Serum proteins: decrease of total serum protein, or reversal of albumin/globulin ratio, while not the sole cause of edema, facilitates its appearance, with symptoms dependent on the tissues involved, central nervous system, anuria, ascites, or general. This appears more commonly with inadequate protein in the diet.

These tests and principles are applied to suspected or potential toxemias and, so far as possible, to these same patients at the end of the puerperium, just preceding discharge from the hospital, and at intervals for years, either in subsequent pregnancies or by hospitalization for a brief period at intervals of three, six, and twelve months, or whenever they can be prevailed upon to submit to the tests. In addition, we are hospitalizing and testing cases with definite toxemias occurring prior to the initiation of this work, and searching for evidence of actual or latent damage.

Outstanding in all this work is the fact that no test or group of tests accurately represents the complete picture of toxemia of pregnancy, and that clinical experience and judgment must not be relegated to a position secondary to any arbitrary set of standards. We are learning to more accurately judge the value of the tests; to discriminate in cases where all findings are not in accord; learning how far cases may be carried without immediate jeopardy to mother or child; what the remote consequences of the prolongation of the toxemic states are; learning the efficacy of the various therapeutic procedures; and discarding from the category of toxemias cases that have previously been so considered.

THERAPY

After complete tests are finished, patients are put on a salt-free diet. During pregnancy there is an invisible edema which is aggravated by the sodium ion, and diuresis and loss of weight occasionally follow this procedure alone. Potassium chloride, 2 to 3 gm. daily, is given on the tray, to be used as salt, and this definitely decreases edema in many instances.

TABLE 1*

PATIENT	DATES	ALBUMIN		BLOOD PRESSURE		ROSE-BENGAL		UREA CLEARANCE PER CENT		EDEMA		PSP	
H.	5/34-4/35	+++	0	130/100	120/ 80	77-50	60-40	44	82	0	0	--	--
B.	5/34-3/35	+++	0	160/100	125/ 80	45-20	50-35	38	74	0	0	--	0
R.	3/35-5/35	0	0	155/100	112/ 74	53-30	--	16	135	+++	0	63	--
D. P.	8/33-3/35	++++	0	200/120	110/ 75	--	--	--	58	++	0	--	--
H. R.	7/33-3/35	++	tr.	110/ 70	120/ 70	--	--	--	85	++	0	58	--
S.	11/33-3/35	+-++	+	180/130	140/100	--	--	85	25	0	0	60	50
S. P.	12/33-4/35	+++	0	170/110	120/ 80	--	--	70	--	++	0	67	--
G.	12/33-4/35	0	0	140/ 90	110/ 80	--	--	--	--	0	0	--	--
Bl.	12/33-4/35	++++	0	170/110	148/ 90	--	--	100	--	++	0	75	--
H. O.	9/33-4/35	++	0	110/ 70	110/ 70	--	--	80	--	0	0	100	--
F.	9/23-3/35	++	0	164/110	115/ 80	--	67-35	--	50	0	0	--	60
O.	1/29-4/35	+++	0	200/130	140/ 90	--	43-28	--	50	++	0	--	63

**Results of retesting after delivery:* First column under each heading is before delivery; second column subsequent to delivery. Cases in which tests were satisfactory were not repeated in some instances.

Case S was allowed to continue pregnancy for four months because of desire for child and now has definite vascular and renal damage. The last two cases had eclampsia in first pregnancies, and again in subsequent pregnancies. At present they show evidence of some damage. All others apparently are normal.

Adequate Protein Diet.—Usually 100 gm. is given daily in women of average weight. If there is excessive loss as urinary protein, additional protein is given. If serum proteins are low, larger protein feedings may raise the level or at least aid in preventing further lowering of this level. Protein is given as meat, milk, eggs, and cheese. There is no evidence that meat in the amounts allowed is harmful.

Fluids are given freely, even in the presence of edema. Since edema is due to tissue thirst, which must be satisfied before there is available much water for renal excretion, toxins can best be washed out by liberal administration of fluid.

Sedatives.—Potassium bromide and barbiturates are used in the preeclamptic stage, particularly the hypertensive type.

Magnesium Sulphate.—Ten per cent solution intravenously is very effective in reducing excessive blood pressure. The result may be brief, in which case the medication may be repeated.

Glucose in 6 per cent or 10 per cent solution intravenously or by multiple needles subcutaneously, is of value in hypoglycemia and anuria, and hypertonic glucose is valuable in edema of the brain accompanying convulsions in eclampsia. By supplying tissues with adequate nourishment, supplemented by small doses of insulin, marked improvement in metabolism may result, releasing water from tissues. A liberal carbohydrate diet is given by mouth, with no attempt to control fetal weight.

Calcium as lactate by mouth, and gluconate or levulinate intravenously protects against liver damage, and by replacing sodium from tissues, promotes diuresis.

Venesection is avoided at all costs. Tissues are suffering from a suboxidative state, and removal of oxygen and food-carrying tissue is harmful to the organism. Other methods for attack of special symptoms should be utilized.

Shock, one of the toxemic manifestations occurring usually just postpartum, occasionally antepartum, is due to rapid loss of blood volume, not as hemorrhage, but depletion of free blood water by tissues. The primary need is a fluid that will remain in the circulation. Salt and glucose solutions are lost almost as rapidly as given. Blood transfusion or acacia solution are the two forms of fluid which conform to these requirements, and improvement during the course of acacia administration is frequently very striking.

To combat the hypotension, adrenalin repeatedly, strychnine in doses of 1/10 grain, and caffeine are all valuable and may be used at the same time. Oxygen is of great assistance in the cyanosis and dyspnea of shock.

The above 62 cases (Tables II and III) constitute the cases of toxemias which manifested symptoms sufficiently severe to warrant hospitalization.

Column A in Table III represents 35 patients in whom toxic manifestations appeared early in pregnancy. These cases were carried along on treatment and had repeated functional tests. When symp-

TABLE II

MATERNAL DEATHS

	NUMBER OF CASES		TOTAL	EXPRESSED IN PER CENT		
	35 A	27 B	62 C	35.0 A	27.0 B	62.0 C
Primipara	12	14	26	34.2	51.8	41.9
Multipara	23	13	36	65.8	48.2	58.1
Spontaneous onset of labor	27	16	43	77.1	59.2	67.7
Induction, castor oil, quinine	5	4	9	14.2	14.8	14.5
Induction by bag	1	1	2	2.8	3.6	3.3
Normal deliveries	24	18	42	68.5	66.6	67.7
Forceps	1	4	5	2.8	14.8	8.0
Breech	2	2	4	5.6	7.2	6.4
Twins	1	0	1	2.8	0	1.6
Version and extraction	1	0	1	2.8	0	1.6
Vaginal hysterotomy, craniotomy	1	0	1	2.8	0	1.6
Cesarean section						
Low cervical	6	2	8	16.8	7.2	12.9
Porro sections	1	0	1	2.8	0	1.6
Indications for section				5.6	7.2	12.9
Pelvic	2	2	4	33.2	66.6	50.0
				2.8	0	1.6
Previous section	1	0	1	16.6	0	12.5
				8.6	0	4.6
Toxemia	3	0	3	49.8	0	37.5

TABLE III

FETAL DEATHS

	NUMBER OF CASES		TOTAL	EXPRESSED IN PER CENT		
	35 A	27 B	62 C	35.0 A	27.0 B	62.0 C
Premature births	13	5	18	27.1	14.7	29.1
Term births	22	22	44	62.9	85.3	70.9
Average weight of babies	6 lb. 4 oz.	6 lb. 1 oz.	6.0 lb. 2.5 oz.			
Gross infant mortality	10	3	13	28.5	11.1	20.9
Term baby deaths	2	0	2	20.0	0	15.3
Premature deaths	8	3	11	80.0	100.0	84.7
Antenatal deaths	3	2	5	30.0	67.0	39.5
Postnatal deaths	7	1	8	70.0	33.0	61.5
Maternal deaths	0	0	0	0	0	0
Sepsis	1	2	3	2.8	7.2	4.9
Eclampsia	2	1	3	5.6	3.6	4.9
Intrapartum	0	1	1	0	3.6	1.6
Postpartum	2	0	2	5.6	0	3.2
Antepartum	0	0	0	0	0	0

toms and tests gave evidence of severe disturbance, pregnancy was terminated artificially in this group. The other patients in this group went into labor spontaneously at term or prematurely. Many of these

cases were carried for months. This group necessarily is composed of the serious types of toxemia.

Column B is composed of 27 patients who, for the most part, exhibited toxic symptoms late in pregnancy. These cases, except for two, were mild toxemias.

The only reason for continuing pregnancy in the face of a toxemia is in interests of the child. It was hoped that by careful clinical observation and frequent functional tests, patients exhibiting a toxic state early in pregnancy could be carried with fair degree of safety to approximately term. This was accomplished in about 60 per cent of the cases. The other patients either delivered prematurely or the pregnancy had to be terminated prematurely.

At the present time, all that can be said for 35 patients in Group A is that about 60 per cent will carry to viability, 40 per cent will deliver prematurely or will necessitate termination of pregnancy before term, 33 per cent will lose their babies, and 20 per cent will probably suffer some latent damage.

CONCLUSIONS

1. Toxemia of pregnancy is a generalized, systemic manifestation of an as yet unknown agent, these manifestations appearing in one or more systems, each with its individual symptoms, with tests more or less specific for each of the systems.

2. There is no test which alone is of value in determining the severity of the condition and each test must be interpreted in the knowledge of the field to which it applies.

3. In the aggregate, the tests enumerated give valuable information regarding the status, progression, value of therapy and degree of recovery. Taken collectively in conjunction with clinical observations, they may safely be the basis of accurate decisions.

Gery, L., and Adrian, J.: Statistical Study of Tumors of the Ovary. Report of Five Hundred Cases, Bull. Soc. d'Obst. et de Gynéc. **24:** 310, 1935.

The authors studied 506 ovarian tumors. In listing them they follow the classification of P. Masson. They found that 42.6 per cent were tumors of the ovarian tissue proper, chiefly cysts; 27 per cent were wolffian tumors; 8.2 per cent mesenchymal newgrowths; 14 per cent cystic teratomas; 2.4 per cent metastases, and in 5.8 per cent the type of tumor could not definitely be determined.

The authors conclude that it is difficult to make a prognosis from the histologic diagnosis. However, of the 506 cases, 51.4 per cent were histologically benign, 38.5 per cent were histologically malignant, and in 10.1 per cent differentiation not definite.

J. P. GREENHILL.

TREATMENT OF VESICOVAGINAL FISTULAS*

Past and Present

Norman F. Miller, M.D., Ann Arbor, Mich.

ALTHOUGH the incidence of vesicovaginal fistulas is not accurately known, there is evidence to warrant a possible belief that its decrease as a result of improved obstetrics is balanced by a higher incidence following pelvic surgery. The fact that, today, large series of cases are seldom reported does not refute this belief. Instead, it may be taken as an indication of the fact that surgeons everywhere are attempting repair of fistulas whereas in former years individuals so afflicted generally gravitated to larger centers where this type of work was being done successfully. Failure following attempt at repair is still common. To this many individuals will testify, and one need only inspect patients' records to realize that many unsuccessful operations may pave the path to ultimate relief. Because of these things and because of a firm belief in the fundamental truth voiced by Dr. George Gray Ward,[152] who seventeen years ago commented thus: "The most successful surgeon of the future will be he who, with a wide knowledge of all the methods at his command, chooses the one which will be most suited to the individual case." I desire to present a survey, a panorama as it were, of the treatment of vesicovaginal fistulas, leaving for another time a similar contribution on the even more interesting group wherein the urethra and bladder sphincter are involved.

While vesicovaginal fistulas have existed since the beginning of mankind, probably the earliest tangible evidence of its occurrence was the discovery by Professor Derry of a large vesicovaginal fistula in the mummy of Queen Henheit, one of the wives of Mentuhotep who reigned about 2050 B.C. (Bey[14]). Hippocrates (460-377 B.C.) mentioned the involuntary discharge of urine following some confinements but said nothing of its cause (Agnew[5]). Bey credits Avicenna (A.D. 1037) with the first accurate description of the lesion. In 1582 Ambrose Pare[5] discussed fistulas in general but did not mention vesicovaginal fistulas. Later in the sixteenth century Louis de Mercado, Felix Plater, and Severin Pineau all gave a clear description of the lesion.[87]

Earliest mention of treatment probably appeared in the Ebers Papyrus (Bey), where several prescriptions are given for the cure of incontinence of urine in women. Aside from spontaneous healing which was probably attributed to the influence of prevailing mystic concoctions of legendary interest, no real step toward the correction of this dreaded condition is recorded until the latter part of the seventeenth century when, in 1672, van Roonhuyse of Amsterdam first presented a well-defined remedial plan.[87] His method is of more than usual

*Presented, by invitation, at a meeting of the New York Obstetrical Society, February 12, 1935.

interest, since it was probably the first recorded operative procedure for vesicovaginal fistulas. Van Roonhuyse advised denudation of the edges of the fistula with scissors or knife and their approximation by use of pins made of strong sharpened goose quills which were properly wrapped with red-waxed silk and coated with a healing salve. Dressings of flat wicks moistened in warm balsam oil were then applied and the vagina filled with suitable sponges moistened in a little oil of sweet almonds (Kelly). Because of his clear description and familiarity with fistulas, Kelly believes van Roonhuyse actually operated upon patients by this technic. About seventy-five years elapsed before the next significant mention of treatment was made. In 1752 Johannes Fatio[87] spoke of pulverizing live toads in a new pot, the product to be placed in a bag and worn around the abdomen; but stated that he preferred surgical methods and mentioned curing several fistulas by the van Roonhuyse technic.

Progress during this earlier period was slow but the darkness was thinning and, at the beginning of the nineteenth century, there dawned a new day in the treatment of vesicovaginal fistulas, which reached its zenith half a century later in the great contributions of Jobert (de Lamballe[76-79]), Wützer,[158, 159] Simon,[137-139] Sims,[140, 141] Brown,[25, 26] Emmet,[50-52] Bozeman[20-24] and others. Prob-

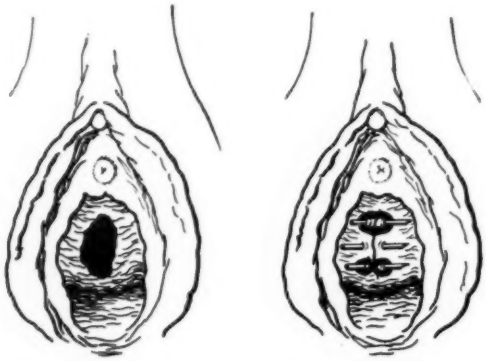

Fig. 1.—The use of sharpened goose quills as a means of approximating the edges represents the earliest type of operative procedure for the correction of vesicovaginal fistula. (Von Roonhuyse, 1672.)

ably the first record of importance in this new era is that of Desault,[9] who in 1804 obstructed the opening with a plug (sphere of gum elastic) or valve covered with wax, using at the same time a large catheter retained in the bladder by means of a truss. About this time Dupuytren first recommended caustics and cautery. Vidal (de Cassis[9]) invented a spring forceps for approximating edges of the fistula, while Naegele[9] (1812) made an extensive study of the condition and attempted repair. Later (1822) he pared the edges and approximated with interrupted sutures. In James'[75] *System of Midwifery*, published in 1813, we find the use of an elastic catheter advised to aid spontaneous healing. James also mentioned using a cautery where the opening was small, and spoke of freshening the edges and employing a catheter where the opening was large. Vidal (de Cassis[9]) recommended closure of the vulva. In 1829 Levert,[122] of Mobile, experimented with metallic sutures and in the same year Malagodi[9] of Bologna pared the edges of fistulas and approximated with suture. Similarly, Diffenbach,[9] using a speculum for better exposure, pared the edges and approximated with lead or wire sutures. Gosset[9, 65] (1834) used gilt wire for closing fistulas. Professor Roux (1829) proposed the knee-elbow posture for better exposure, but postural exposure and the gutter speculum are thought to have been

known and used by Schreger as early as 1817. Soon afterward posture was adopted by Ryan[130] and by Wützer[158, 159] (1834).

Barter[122] (1836) placed patients in the knee-elbow position when cauterizing fistulas, and Liston mentions the use of this position in 1838. In Dantzig, Wagner[9] (1834) described splitting the posterior edge of the opening and placing in this cleft the beveled anterior edge. In the same year, Wützer of Bonn systematized the operative treatment and emphasized the importance of posture for exposure during operation as well as for drainage during the postoperative period. He not only pared the edges of the fistula and approximated with suture using knee-elbow posture for exposure but performed suprapubic paracentesis and kept the patient on her abdomen during the postoperative period for better drainage. In 1848 Wützer reported eighteen patients operated upon, with three cures.

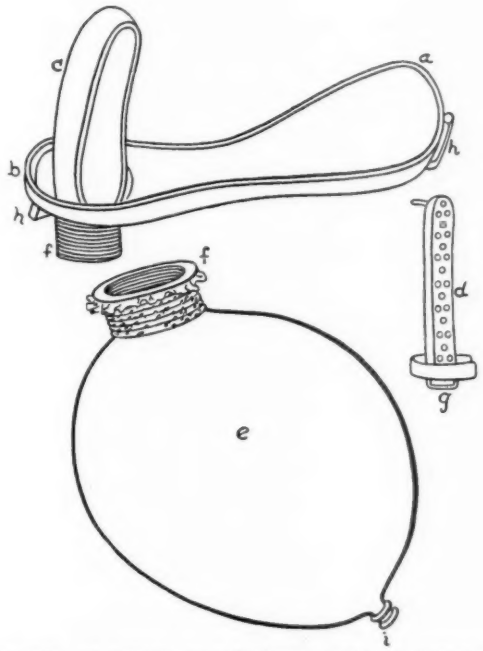

Fig. 2.—This early type of urinal was designed with an intravaginal extension to fit over the opening of the fistula.

In our own country the first record of operative closure is attributed to Hayworth,[9, 5] who (1839) freshened the edges of the fistula and approximated with thread sutures. Later he reported a total of twenty patients treated with three cures (Agnew[5]).

In 1846 Metzler[9] of Prague combined many of the suggestions made up to that time. He placed his patients in the knee-elbow position, used a right-angled speculum, and approximated the denuded edges with gilded needles held in place by clamps of shot. Postoperative drainage was provided by a catheter in the bladder. In the same year, Pancoast in Philadelphia used a split flap method. Mettauer[122] in Virginia used lead wire for approximating the edges. Luke[9] of Charing Cross Hospital used silver wire for the same purpose in 1850.

Interest in the treatment of vesicovaginal fistula had now gained considerable momentum and much credit for this must go to Jobert (de Lamballe)[76-79] of Paris who about 1834 attempted to transplant tissue flaps from the vulva as a stop-gap.

In 1845 he cut the bladder free from the cervix in order to minimize tension and in 1849 reported thirteen cures. He was perhaps the first to emphasize the importance of avoiding tension. To this end he not only attempted mobilization of the bladder but made incisions in the vaginal mucous membrane. Maisonneuve, following the teaching of Jobert (de Lamballe), was able to cure a case where the whole anterior wall of the vagina had disappeared.

Nearing the peak of this new era, we now find Simon,[137-139] in Germany, following the precepts of Jobert but improving upon his technic by substituting tension sutures for vaginal incisions. Simon became a recognized leader in this type of work. In 1854 he was able to report cure in thirty-five of forty patients operated upon. Simon, interestingly enough, used an exaggerated lithotomy

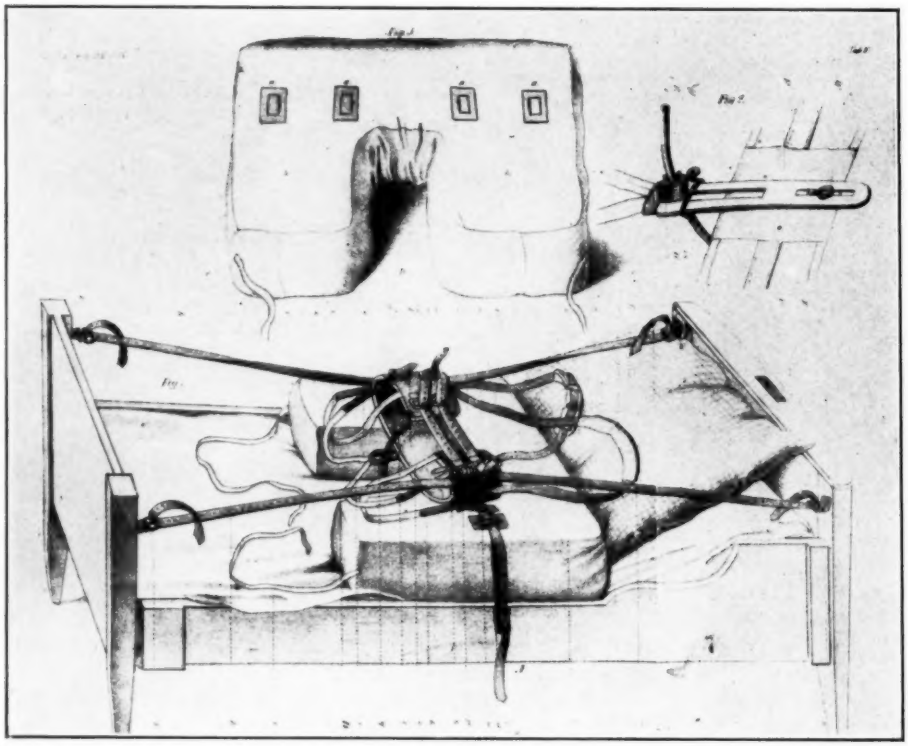

Fig. 3.—Bed and harness designed in 1842 by the unrecognized genius Wützer, for the purpose of maintaining the patient in the knee-chest position during the long exhausting time required for operation.

position and paid little attention to postoperative care, using no drainage and often permitting his patients to be up a few days following operation. About this time America was destined to witness the début of one of its most famous surgeons. For in 1852 J. Marion Sims'[141] now famous article, "On the Treatment of Vesico-Vaginal Fistula," appeared in the *American Journal of the Medical Sciences.* Sims quickly became a recognized master in this work, his fame spreading the world over. He emphasized adequate exposure which he obtained by use of the "Sims' speculum" and "Sims' position." Denudation of the edges and approximation with silver wire were essential parts of his technic. Postoperatively he considered five things important: (a) The use of a block tin catheter for continuous drainage; (b) bowel to be kept quiescent for ten to

fifteen days; (c) opium; (d) normal fluids, (e) perineal irrigations. The success of this remarkable surgeon will be more fully grasped when we realize that eight years after his initial operation he was able to report on a series of 261 cases with cure in 81.9 per cent (Rawls[125]). The fascinating story of his trials and worries is to be found in his publications and in the story of his life. The fact that after forty operations on his first three patients he failed to achieve a cure, shows that his rise to fame was not without struggle and tenacity of purpose on his part. In Thomas Addis Emmet,[50-52] Sims' successor at Woman's Hospital, New York, the world was quick to recognize a master of the highest caliber. So skillful did Emmet become in the treatment of vesicovaginal fistulas

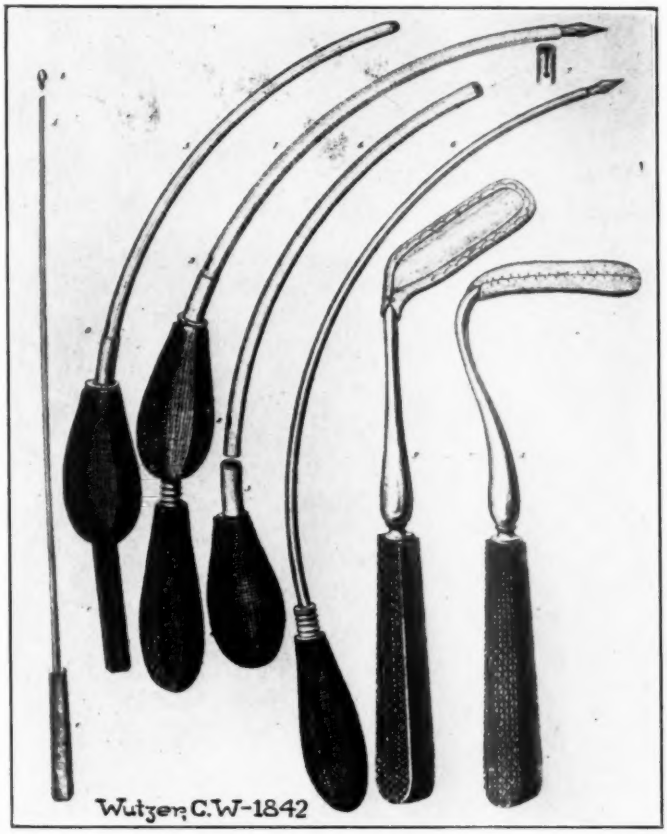

Fig. 4.—Instruments designed by Wützer. Note trocars used for suprapubic drainage.

that his record has stood the test of time and with few exceptions has never been equaled. The remaining decades of the nineteenth century are studded with reports on the subject, each adding in its own way to the rapid progress which now characterized the treatment of vesicovaginal fistulas.

Fortunately, perhaps for us and for patients afflicted with bladder injuries, so intense did the interest in vesicovaginal fistulas become that there developed a vigorous controversy over the best method of treatment. Leading participants in this controversy were Simon in Germany, and Bozeman[20-24] in this country. The literature of their day is replete with interesting side lights involving these men and their pet methods. Bozeman was tenacious and loyal to his "button"

suture (consisting of silver wire employed in the manner of Sims but held in place by a small perforated lead clamp or "button" through which the wire ends passed) for which he claimed better coaptation of the fistulous edges. The idea was ingenious and in the hands of this remarkable surgeon gave enviable results. Bozeman used a knee-elbow position for his patients when operating, and like most American surgeons of his day laid considerable stress on proper preoperative preparation. This included local hygiene leading to healthier tissue and incision of cicatricial bands to permit mobilization of the fistula. Readers

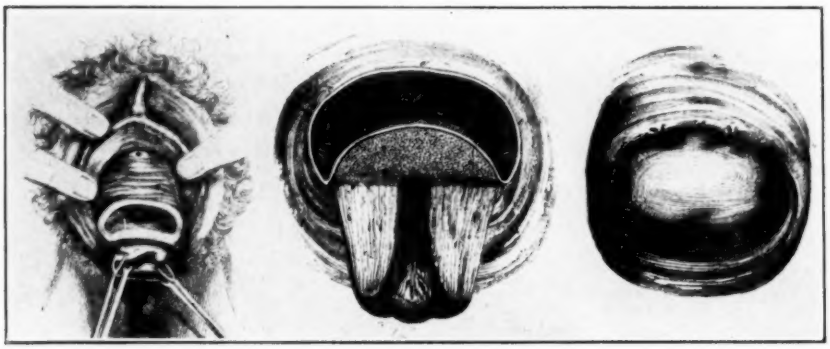

Fig. 5.—Closure of fistula by using cervix as a stop-gap. This technic was used by Jobert de Lamballe in 1852, and is described in his book entitled *Traité des Fistules Vesico-Uterines.*

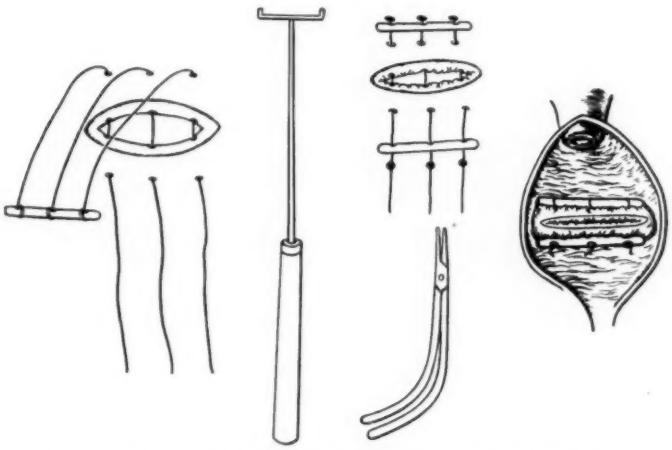

Fig. 6.—The use of wire was not original with Sims, but to him goes the credit of popularizing this method of closure in America.

of medical history may well linger with these masters in the closing years of the nineteenth century, for few surgical developments are illuminated by more interesting side lights.

In 1890 Trendelenburg[146] attempted to repair a vesicovaginal fistula by the suprapubic route. With this new avenue of approach dawned our modern and more versatile era in the treatment of this condition. So intense was the stimulus engendered by the leaders in this type of surgery that in 1906 Kelly[86] was able to report a variety of approaches for the correction of vesicovaginal fistulas including: (A) Parasacral route (Kraske's), (B) ischiorectal route (Michaux), (C) transperitoneal route (Sanger), (D) paravaginal route (Schuchardt's In-

cision), (E) vaginal route (Jobert de Lamballe, Sims, Simon), (F) transvulval or episial route, (G) transurethral route (Kolischer), (H) vestibular route (Jobert de Lamballe), (I) transpubic route (removing a pubic ramus) (Samter), (J) transsymphyseal route (Bramann, Wickhoff), (K) suprapubic extraperitoneal (Trendelenburg), (L) transvesical, transperitoneal (Von Dittel and others).

Most of the approaches named by Kelly were destined to be short lived or perhaps reserved for selected cases. Only the vaginal, the su-

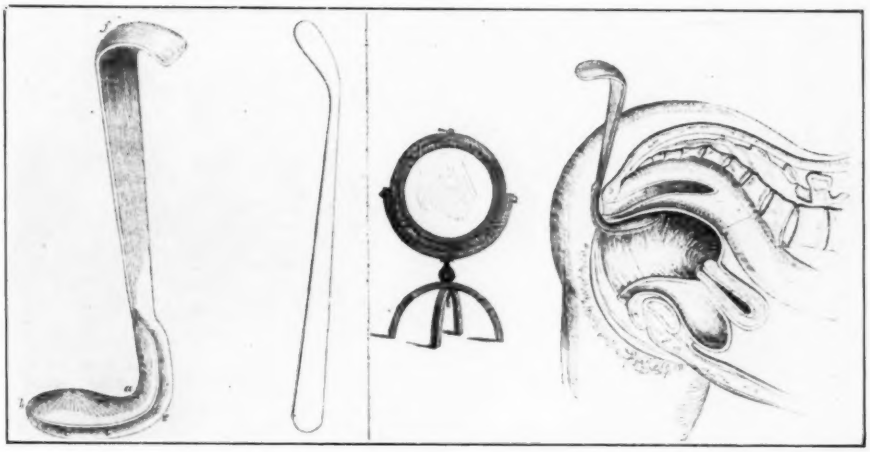

Fig. 7.—Adequate lighting is no longer a major problem, but a century ago it was one of the obstacles to successful treatment. Sims minimized this problem by using reflected sunlight.

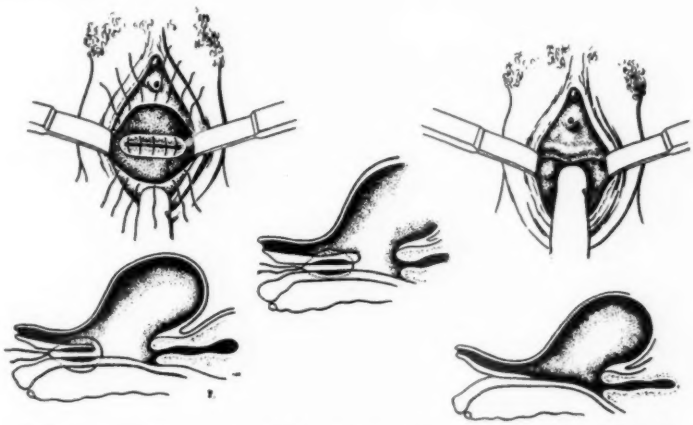

Fig. 8.—Simon, another great leader in the treatment of bladder fistulas, was a contemporary of Sims, Bozeman and Brown. Closure of the vagina as first devised by Maisonneuve was also advocated by Simon. His technic is shown above.

prapubic, transvesical, and transabdominal are accepted today as sound and practicable. Although interest in the suprapubic approach was slow in developing, its progress has been steady, and today we find the transvesical suprapubic approach ranking second in popularity. The gradual favoring of the suprapubic approach may be attributed to the fact that fistulas today are commonly the result of surgical trauma, and

frequently less accessible than those resulting from parturition, especially in cases where total hysterectomy has been performed. Perhaps another reason for the increased interest in the suprapubic route may be found in the fact that urologists are more frequently consulted than in former years.

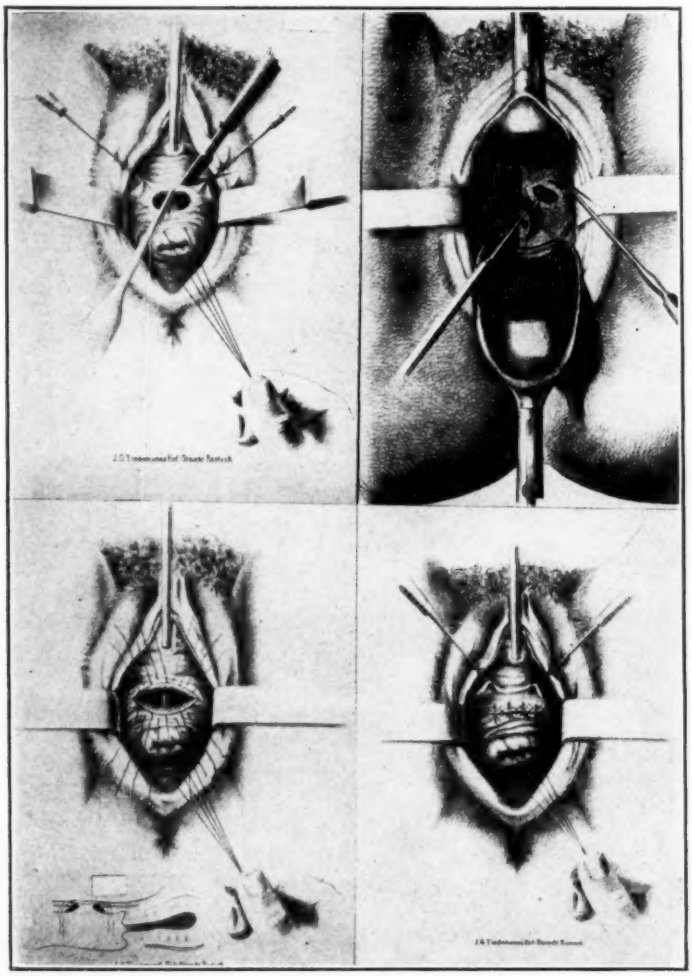

Fig. 9.—Technic used by Simon in repair of bladder fistula as described in his text *Operation der Blasen Scheidenfisteln.*

Revival of the transabdominal route of Sanger and Von Dittel[42, 43] was given a real stimulus by Légueu,[96, 97] who in 1929 reported 89 per cent cures by this approach. The higher mortality connected with this method is a factor to be considered in selecting a suitable technic.

Contemporary treatment of vesicovaginal fistulas may best be characterized by (1) variety of approach, (2) emphasis on mobilization of bladder and vaginal mucous membranes, (3) a general but not unanimous

Fig. 10.

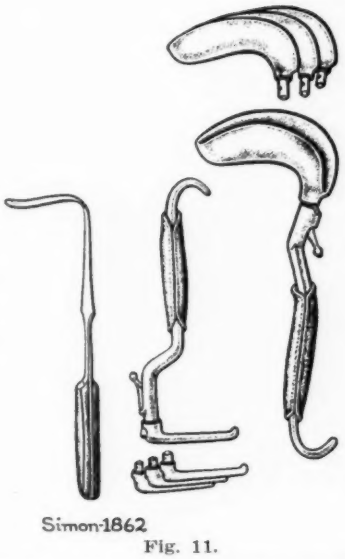

Fig. 11.

Fig. 10.—Simon preferred his patients in the exaggerated lithotomy position when operating for vesicovaginal fistula. This figure taken from an old wood cut portrays the operating room set-up of Simon's time.

Fig. 11.—Like his contemporaries Simon also devised his own instruments. Shown here are the retractors designed and used by him in 1862.

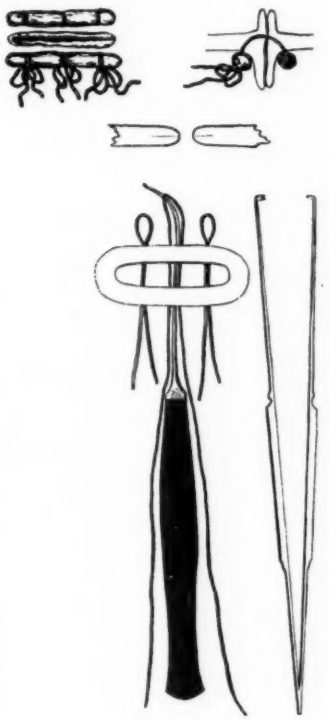

Fig. 12.

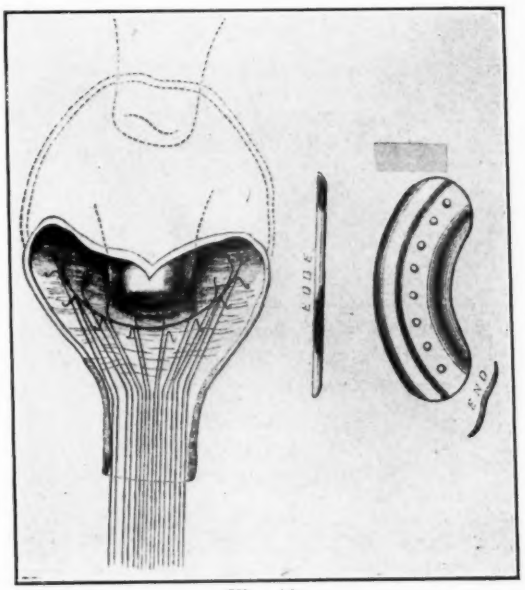

Fig. 13.

Fig. 12.—Technic and instruments used by Maurice H. Collis, Irish surgeon, in the treatment of fistulas.

Fig. 13.—Bozeman, a contemporary of Sims, achieved great success in the treatment of vesicovaginal fistula. Much of this he attributed to the use of so-called "buttons" by means of which he successfully kept the denuded edges of the fistula in close approximation. This figure shows one of these buttons.

trend away from the use of silver wire, and (4) condemnation of colpoclesis. Except for versatility in mode of approach no new stop-gaps

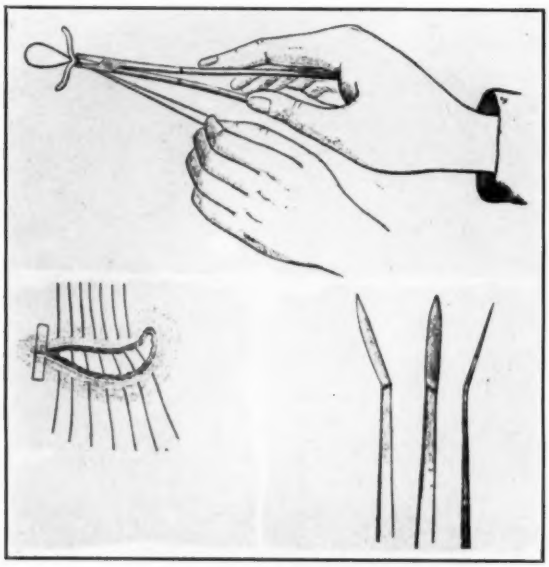

Fig. 14.—Brown, an English contemporary of Sims, Simon and Bozeman, achieved marked success in the treatment of vesicovaginal fistulas. He, too, preferred silver wire and, like many other successful gynecologists, devised many of his own instruments.

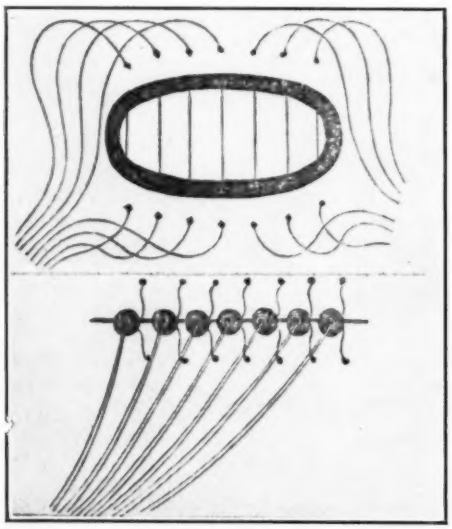

Fig. 15.—Perforated lead shot through which the ends of silver wire were drawn was the usual method of locking the stitches in situ. This is clearly shown in this diagram taken from Agnew.

are recorded. The cervix, uterus, omentum, or muscle are still used to cover the opening when there exists no possibility of mobilizing the bladder base sufficiently to close it. In the smaller fistulas, cautery, now,

however, by electrocoagulation, is again being revived with some success. While the new avenues of approach have undoubtedly made possible a cure in many otherwise intractable cases, we cannot overlook the fact that hundreds of fistulas have been cured by operations through the

Fig. 16.

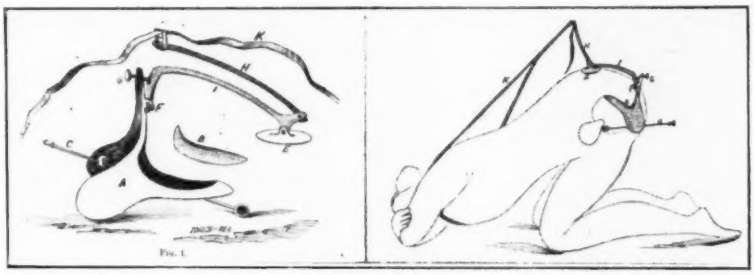

Fig. 17.

Figs. 16 and 17.—Many retractors and speculums were designed to meet the problem of adequate exposure. The self-retaining retractor designed by Erich and the adjustable speculum used by Estes are excellent examples of the ingenuity displayed by the pioneers in this type of work.

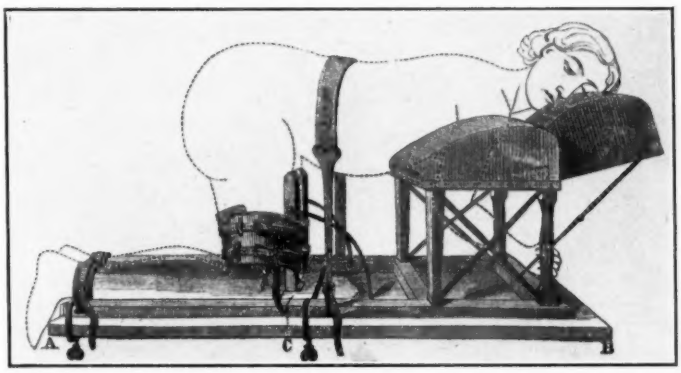

Fig. 18.—Harness and rest used by Bozeman. Compare with bed and harness designed by Wützer in 1842.

vagina and in all probability this will continue to be the preferred method for a long time to come. Still, it is probably fortunate that both routes are being developed, for there certainly can be no good reason to oppose any safe approach of proved value. The contributions of

Trendelenburg,[146] Meyers,[135] McGill,[135] Thiers,[135] Kelly,[84] Everke,[135] Marion,[135] Young,[160] Sears,[135] and others have shown conclusively that the suprapubic transvesical approach is entirely feasible; and Légueu's[97]

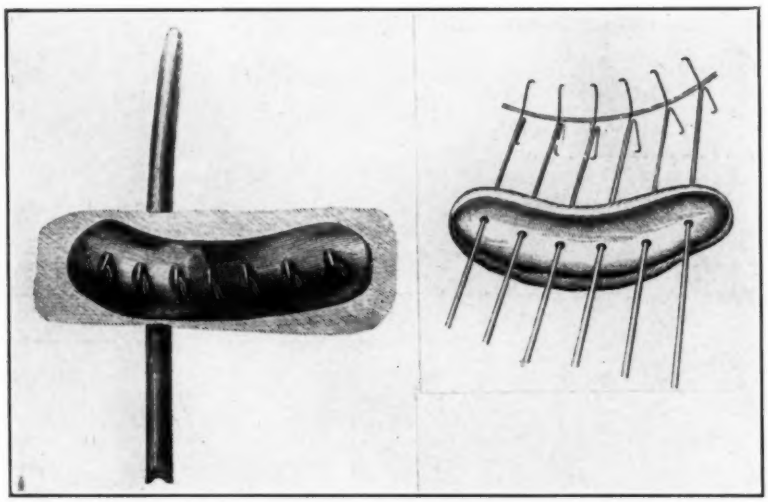

Fig. 19.—"Button" used by Bozeman. Much of his success in treating vesicovaginal fistulas was attributed to their use.

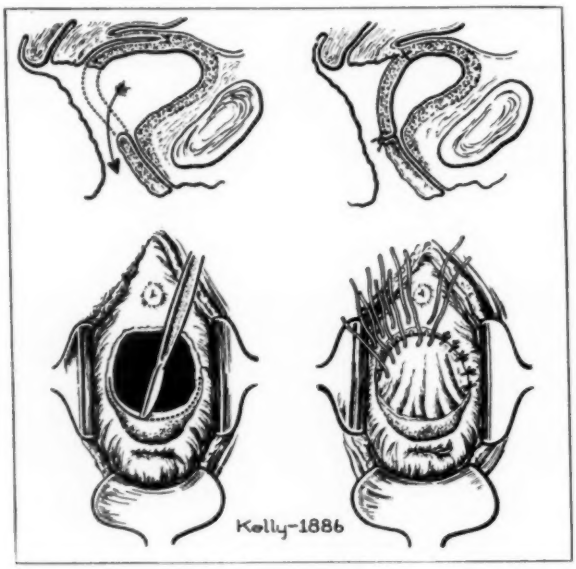

Fig. 20.—Technic used by Kelly in patients with very large fistulas.

technic for the transperitioneal approach may well be considered in selected cases. While my own preference is for the vaginal route, I should have no hesitancy in adopting such other approach as might seem indicated in a given case.

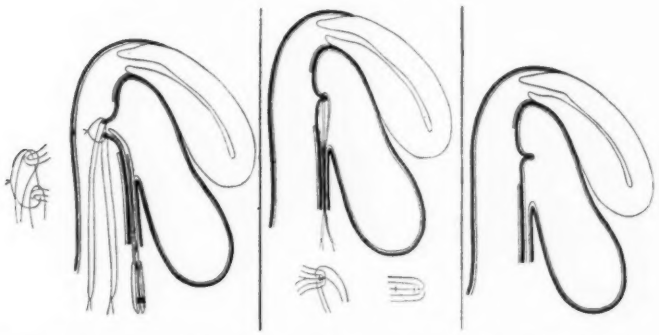

Fig. 21.—Inversion of the edges of the fistula as suggested by Bishop in 1897 sometimes finds advantageous use today.

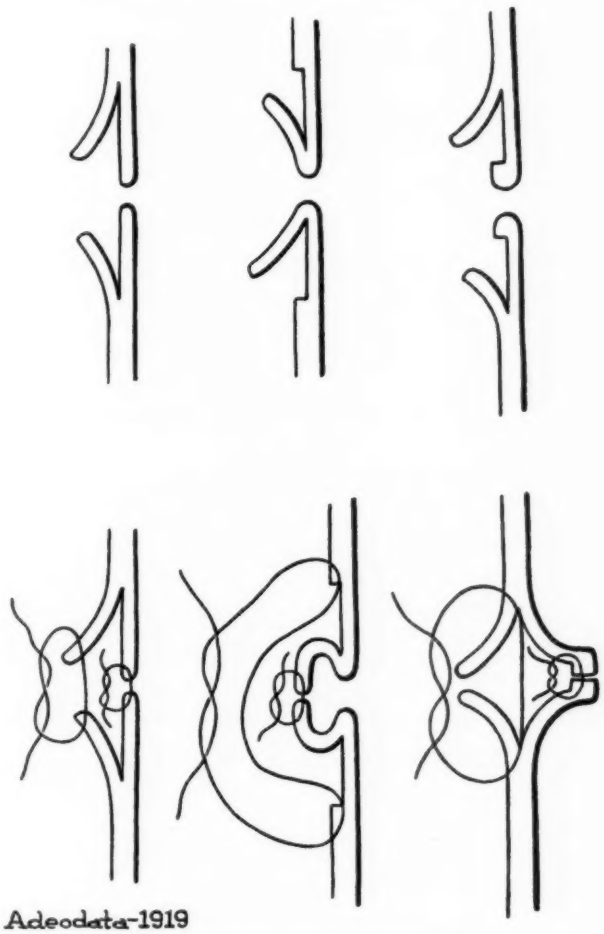

Fig. 22.—The amount of tissue available often determines how the edges of the fistula shall be treated. Several methods suggested by Adeodata are shown here.

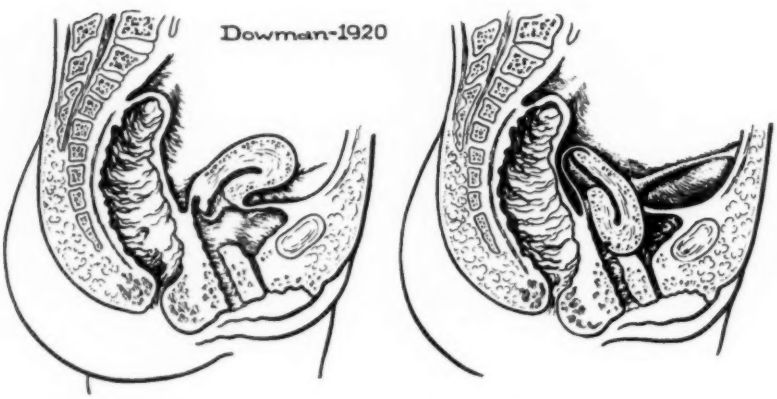

Fig. 23.—Many structures have been used to plug the opening. The cervix was commonly used for this purpose. Use of the uterine body as a stop-gap was suggested by Dowman in 1920.

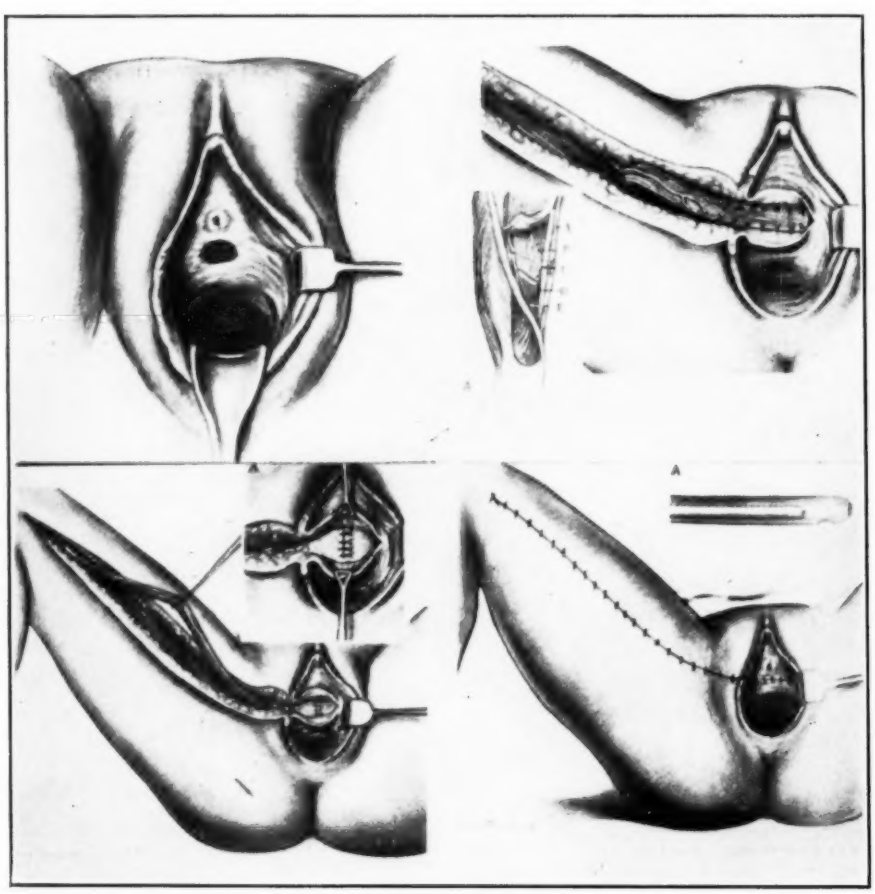

Fig. 24.—Another example of a borrowed stopper is seen in the use of the gracilis muscle as advocated by Garlook in 1928.

Mobilization of the bladder and vaginal mucous membrane has come to be considered a fundamental in present-day treatment. By such methods it is likely that patients have been saved long drawn out preliminary stages when cicatricial bands and scarred areas were prepared for operation. Mobilization is important, for union seldom occurs in the presence of excessive tension. I am not, however, satisfied that the present cry for mobilization is not occasionally over-loud. Slough, resulting from excessive trauma incident to mobilization of badly scarred tissues, with unsuccessful union frequently occurs. Perhaps in cases of excessive scarring, it would be wiser to relieve tension by more remote incisions, leaving the poorly vascularized tissues intact and free from tension. Certainly the results of our illustrious predecessors of the last century have amply demonstrated the practicability of relieving tension in that manner.

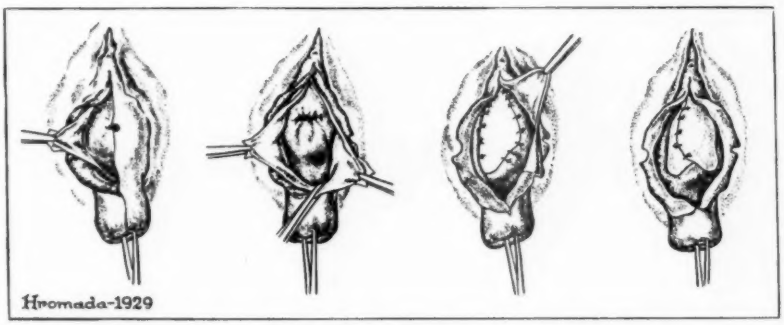

Fig. 25.—Unfortunately the method here shown cannot be utilized readily when the uterus has been removed and the fistula is located high in the vaginal apex.

The trend away from the use of silver wire was natural, paralleling the general use of catgut in other fields of surgery. The wisdom of the change from wire to catgut in the correction of vesicovaginal fistulas has been justly questioned more than once. The almost unparalleled record of Sims, Emmet, Bozeman, staunch advocates of silver wire, scarcely justifies its present consignment to oblivion. Too frequently we do what is being done, never pausing in our acceptance to consider the matter in the light of its true merits. I have never used silver wire and cannot, therefore, speak from experience. It does not appear, however, that the career of catgut as successor to silver wire in the treatment of vesicovaginal fistulas has been characterized by anything remarkable.

Colpoclesis or closure of the vagina, first proposed by Vidal, was a real boon to older women with incurable vesicovaginal fistulas. The high or transverse obliteration of the vagina was used by Simon as early as 1856. Opposition to colpoclesis was voiced during the late years of the nineteenth century, but its complete elimination probably did not occur until Coffey made his great contribution on ureterointestinal anastomosis.

While we look with intolerance upon colpoclesis today, it must be remembered that this was once an operation of inestimable benefit to women with incurable fistulas.

STATISTICS

Statistics on the results of treatment in vesicovaginal fistulas are numerous. They range from small series up to 300 and cures rise as high as 95 per cent (Bey). Obviously, however, these results are not

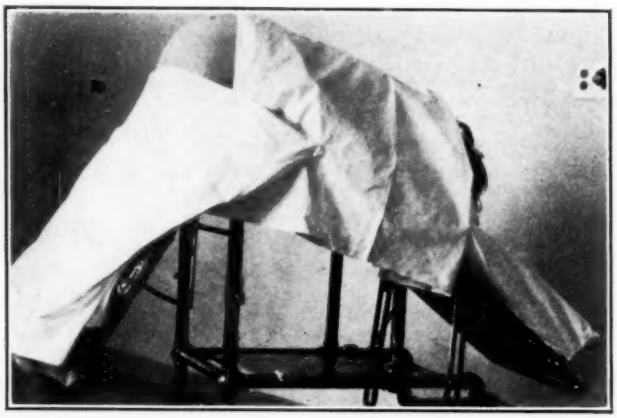

Fig. 26.—With the patient in the inverted Trendelenburg position, good exposure can be obtained by retracting the perineum with a Sims speculum. This permits the operator to look down on the field of operation and tends to minimize technical difficulties.

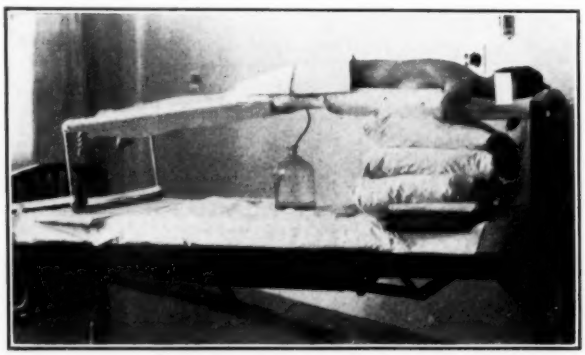

Fig. 27.—When the patient is kept in the prone position following operation, the site of repair is above the urinary pool and gross soiling of the operative site is minimized. Patients are kept in this position for ten days following operation.

easily compared. So many factors must be taken into consideration that one even hesitates to attempt comparisons. In every series the results will depend on certain controllable factors including: (a) skill and technic of the operator, (b) health of tissues, and (c) infection; and upon certain noncontrollable factors as: (a) size of fistulas, (b) location, (c) involvement of other structures, cervix, ureters, urethra, bladder sphincter, etc., and (d) amount of scar tissue. Furthermore

the criteria for cure are not constant and the number of operations necessary to accomplish cure may or may not have been a consideration. The results are often recorded as "satisfactory," an elastic term which may include individuals who, though much improved, still have slight leakage. It would seem that a speedier appraisal of our modern methods of treatment could be achieved were reports to list as cures only those cases where complete healing without leakage obtains. The number of operations required to achieve success should be recorded. Complications should be stated and those involving the urethra, for example, should be listed separately. Certainly cure of the average uncomplicated vesicovaginal fistula is not to be compared with the difficulties encountered in correcting fistulas involving the urethra and bladder sphincter. The statistics given here are by no means complete, but include a sufficient sampling from earlier and present times to permit crude comparison. Space will not permit inclusion of the comprehensive collection of 201 cases (all kinds) reported by Neugebauer in 1891. This interesting compilation is, in a sense, an important historical document covering the problems, operations, and results of the pioneers in the treatment of vesicovaginal fistulas.

STATISTICS

NAME	YEAR	NO. CASES	ROUTE	CURES	PER CENT
Simon	1854	40	Vaginal	35	87.5
Sims	1860	261	Vaginal	216	82.7
Brown	1863	60	Vaginal	50	83.0
Simon	1869	105	Vaginal	92	89.5
Heppner	1869	22	Vaginal	15	68.0
Emmet	1878	171	Vesico- and recto-vaginal	149	87.1
Toth	1909	131			71.5
Bentall	1910	21			63.0
Frank (Mt. Sinai Hosp.)	1917	19	Vaginal chiefly	14	73.6
Judd (Mayo Clinic)	1920	56	Vaginal chiefly	42	82.0
Mackenzie (Royal Victoria Hosp.)	1922	10	Vaginal chiefly	8	80.0
Schroeder	1922	19	Vaginal chiefly	16	84.0
Saenger (Second Univ. Clinic, Munich)	1929	13	Vaginal chiefly	12	92.3
Sears	1929	50 (collected)	Transvesical	40	80.0
Légueu	1928	24	Transvesical		64.0
			Transabdominal		89.0
Bey	1929	276	Vaginal chiefly		86.5
Bey	1930	300	Vaginal chiefly		87.0
	Last	100	Vaginal chiefly		95.0
Lower	1930	27	Vaginal chiefly		90.0
Apajalahi (Univ. Clinic) (Prof. Engstrom Clinic)	1931	159	Vaginal chiefly	118	74.0
Rawls	1931	149	Vesicovaginal and rectovaginal	86	74.8
Rawls	1934	23	Vaginal	21	91.3

In my own practice a variety of procedures have been tried, from mobilization of bladder and vaginal mucous membranes and approximation, to plugging the opening with the uterus. Since July, 1931, however, a constant method has been used based on the principles that healing is dependent upon:

(1) The presence of healthy tissue (healthy scar tissue included), (2) good blood supply, (3) lack of tension, (4) absence of gross infection, (5) avoidance of gross wetness.

The technic I now use is a composite of many older methods. Briefly, it consists of the following:

Preparation: (1) Preoperative preparation: Local hygiene, douches, baths, local application of antiseptics, if necessary. (2) Urinary antisepsis*: Fluids not forced, ammonium chloride and urotropin each, gr. v. four times daily. (3) Bladder irrigations if indicated. (4) Cystoscopic with localization of ureteral orifices.

If the health of the tissue is good, this preliminary preparation may last but a few days. If, however, the local hygiene is poor, the tissues edematous and the injury recent, the patient may be sent home to carry on as outlined above until at least three months have elapsed since the injury was sustained.

Operation.—

1. Inverted Trendelenburg position; prone with head down. (In our small series many positions have been tried but this position has always proved most helpful.)
2. Mobilization of bladder and vaginal mucous membranes. (When tissues are badly scarred, trauma and damage to poorly vascularized tissue is lessened by remote mobilization.)
3. Inversion of bladder mucous membranes and eversion of vaginal mucous membranes when possible; twenty-day chromic catgut No. 1 or 0 being used.

Postoperative.—

1. Prone position on well-padded frame for ten days.
2. Indwelling catheter in bladder with daily boric irrigations. (I am well aware of the divided opinion concerning the use of a catheter for postoperative drainage but feel that no good argument against its use has yet been raised and in our experience it has been of real benefit.)
3. Normal amount of clear fluids only (not forced).
4. Urotropin gr. v, ammonium chloride gr. v, four times daily.

By using this position the repaired wall of the bladder is "on top" and though moisture cannot be prevented, the site of operation at least is not at the bottom of the bladder pool.

RESULTS

Thirteen consecutive vesicovaginal fistulas, varying in size from pinpoint to two inches in length, have been treated in this manner. The last and most difficult was fixed to the left pubic ramus and densely scarred, a case very similar, I believe, to that reported by Phaneuf in 1933.

Most of these fistulas were small, but this is not always a good criterion as to ease of closure. No 13 was particularly difficult because of its location behind the left pubic ramus and the scar tissue, while No. 1 though two inches in length was easy to close.

*See article, *Miller and Chu:* Am. J. Surg. 23: 457, 1934.

No one familiar with the history of vesicovaginal fistulas and the large series of cases reported by the early masters in this line of work can feel other than humble when venturing to record a small series of thirteen consecutive cases such as I have done here. I am not deluded by the fact that twelve patients have been healed following a single operation in each instance (No. 13 is still convalescent in the hospital) for I know full well that this is a coincidence and that all too soon failures will occur. I sincerely believe, however, that the plan of treatment outlined combines desirable features which favor primary healing.

SUMMARY OF OPERATIONS BY AUTHOR'S TECHNIC

NO.	SIZE INCHES	COMPLICATION	ETIOLOGY	NO. OF OPERATIONS ELSEWHERE PRIOR TO ADMISSION	NO. HERE	RESULTS
1	2		Parturition	0	1	Cure
2	¼	Prev. panhysterectomy	Operation	2 cautery	1	Cure
3	⅛	2¼-inch fistula vag. apex. Hysterectomy	Operation	0	1	Cure
4	¼		Operation	0	1	Cure
5	¼		Parturition	1	1	Cure
6	½-⅛	Radium. Panhysterectomy. Double fistulas far apart. Treated separately at same operation	Operation	0	1	Cure
7	¼	Panhysterectomy	Operation	2	1	Cure
8	Very small		Parturition	1 oper. 1 cautery	1	Cure
9	¼		Parturition	0	1	Cure
10	¼		Parturition	0	1	Cure
11	½		Parturition	0	1	Cure
12	Very small	Panhysterectomy	Operation	0	1	Cure
13	½	Behind left pubic ramus	Parturition	0	1	Cure

In presenting this subject I have tried to bring to a focus those methods of treatment which appear most practical either by virtue of results produced or soundness of principle or both. By so doing, I may have made it a little easier to fulfill the prerequisites of a successful surgeon in this type of work.

NOTE: Since this paper was read two additional patients have been operated upon, with cure in each case.

REFERENCES

(1) *Abadie, J.:* Cong. Franc. de Chir. **29:** 549, 1920. (2) *Adeodato, J:* Brazil med. **33:** 273, 1919. (3) *Agnew, D. H.:* Med. & Surg. Rep. **1:** 339, 1859. (4) *Idem:* **6:** 572, 1861. (5) *Idem:* **15:** 1, 57, 115, 190, 272, 309, 328, 373, 391, 413, and 478, 1866. (6) *Allen, T. J.:* New Orleans M. & S. J. **16:** 33, 1888. (7) *Ashe, E. O.:* Brit. M. J. **1:** 275, 1924. (8) *Assaki:* Ann. d. mal. d.

org. gen. ur., Par. 14: 1072, 1896. (9) *Bartlett, J. K.:* Trans. Wis. St. M. S. 5: 67, 1871. (10) *Baumm, P.:* Arch. f. Gynäk. 39: 492, 1891. (11) *Bégouin:* Bull. Soc. d'obst. et de gynéc. de Paris 22: 54, 1933. (12) *Bentall, W. C.:* Lancet 2: 796, 1910. (13) *Berger, P.:* Bull. et mém. Soc. de chir. de Paris 23: 142, 1897.)14) *Bey, Mahfouz:* J. Obst. & Gynec. Brit. Emp. 37: 566, 1930. (15) *Bishop, E. S.:* Trans. M. Soc. 20: 123, 1897. (16) *Bissell, Dougal:* Am. J. Surg. 7: 143, 1929. (17) *Bloch, Jacques-Charles:* Médecine 9: 529, 1927. (18) *Bond, C. J.:* Ann. Surg. 20: 392, 1894. (19) *Bonnet, Louis:* Bull. et mém. Soc. de chir. de Paris 20: 673, 1928. (20) *Bozeman, Nathan:* N. A. M. Chir. Rev. 1: 576 and 885, 1857. (21) *Idem:* Med. Rec. 2: 433, 1867. (22) *Idem:* New York M. J. 8: 484, 1869. (23) *Idem:* Am. J. M. Sc. 60: 100, 1870. (24) *Idem:* Internat. J. Surg. 21: 10, 1911. (25) *Brown, I. B.:* Lancet 2: 581, 1859. (26) *Idem:* On Surgical Diseases of Women, ed. 2, London, 1861, J. W. Davies. (27) *Idem:* Obst. Trans. 5: 25, 1863. (28) *Brownson, J. J.:* M. Prog. 67: 174, 1895. (29) *Bruhl, G. C.:* Cincinnati M. Observer 2: 546, 1857. (30) *Caffier, P.:* Ber. ü. d. ges. Gynäk. u. Geburtsh. 27: 593, 1934. (31) *Carstens, J. H.:* Med. Age 3: 126, 1885. (32) *Cassan:* Gaz. d. hôp. 45: 754, 1872. (33) *Caulk, J. R.:* South. M. J. 13: 116, 1920. (34) *Cazin:* Arch. gen. de med. 1: 275 and 436, 1881. (35) *Chacón, Fr. De P.:* Gac. méd. de México 23: 247, 1888. (36) *Child, C. G., Jr.:* Am. J. Obst. 76: 455, 1917. (37) *Chute, A. L.:* J. Urol. 6: 77, 1921. (38) *Collis, M. H.:* Dublin J. M. Sc. 23: 119, 1857. (39) *Croasdale, H. T.:* Boston M. & S. J. 110: 516, 1884. (40) *Delaunay, E.:* Paris Chir. 18: 203, 1926. (41) *Dieffenbach, J. F.:* Med. Ztg. 5: 117, 173, 177, 1836. (42) *von Dittel:* Med. Jahrb. p. 563, 1881. (43) *Idem:* Wien. klin. Wchnschr. 6: 449, 1893. (44) *Döderlein, A.:* Ztschr. f. Urol. 23: 453, 1929. (45) *Dowman, C. E.:* Surg. Gynec. Obst. 30: 403, 1920. (46) *Dudley, E. T.:* Nashville, Am. J. Surg. & Gynec. 12: 169, 1898/99. (47) *Duplay:* Gaz. méd. de France 59: 85, 1888. (48) *Eastman, J. R.:* J. Indiana M. A. 13: 393, 1920. (49) *Ehrendörfer:* Wien. klin. Wchnschr. 11: 527, 1898. (50) *Emmet, T. A.:* Vesico-vaginal Fistula From Parturition and Other Causes; With Cases of Recto-vaginal Fistula, New York, 1868, W. Wood & Co. (51) *Idem:* Tr. Am. Gynec. Soc. 3: 114, 1878. (52) *Idem:* Am. J. Obst. 31: 593, 1895. (53) *Erich, A. F.:* New York M. J. 8: 478, 1869. (54) *Estes, H.:* New Orleans M. & S. J. 17: 792, 1860. (55) *Eve, P. F.:* Gaz. méd. de France 11: 166, 1860. (56) *Farman, Franklin, and Thompson, R. C.:* J. Urol. 20: 663, 1928. (57) *Flaischlen, Nicolaus:* Zentralbl. f. Gynäk. 19: 1086, 1895. (58) *Frankel, L.:* Zentralbl. f. Gynäk. 48: 2562, 1924. (59) *Frank, R. T.:* Am. J. Obst. & Gynec. 24: 411, 1932. (60) *Freund, R.:* Chirurg. 1: 205, 1928/29. (61) *Garfunkel, Paul:* Zentralbl. f. Gynäk. 49: 2307, 1925. (62) *Garlock, J. A.:* Surg. Gynec. Obst. 47: 255, 1928. (63) *Gayet:* Lyon Chir. 29: 119, 1931. (64) *Goodell, William:* Am. J. Obst. 16: 742, 1883. (65) *Gosset, J.:* Lancet 1: 345, 1834. (66) *Graff, E.:* Wien. klin. Wchnschr. 75: 2392, 1925. (67) *Graham, H.:* Lancet 1: 228, 1841. (68) *Greene, W. W.:* M. Rec. 1: 465, 1866. (69) *Halban, J.:* Zentralbl. f. Bakteriol. 47: 588, 1923. (70) *Hanks, H. T.:* Internat. J. Surg. & Antisept. 1: 132, 1888. (71) *Heppner, C. L.:* Monatschr. f. Geburtsh. u. Frauenkr. 33: 95, 1869. (72) *Herrgott:* Rev. de chir. Par. 4: 574, 1884. (73) *Hirst, C. B.:* Ann. Gynec. & Pediat. 4: 365, 1890/91. (74) *Hromada, Gebhard:* Zentralbl. f. Gynäk. 53: 1431, 1929. (75) *Jacoby, M.:* Ztschr. f. Urol. 25: 529, 1931. (76) *Jobert, A. J.:* Gaz. d. hôp. 8: 405 and 437, 1834. (77) *Jobert, A. J.:* Bull. Acad. Roy. de méd., Paris 2: 581, 1837/38. (78) *Idem:* Traité des fistules vesico-utérines, Paris, 1852, J. B. Baillière. (79) *Idem:* Gaz. d. hôp. 8: 405 and 437, 1854. (80) *Judd, E. S.:* Surg. Gynec. Obst. 30: 447, 1920. (81) *Judd, E. S., and Waldron, G. W.:* S. Clin, J. N. A. 14: 551, 1934. (82) *Kahn, Emanuel:* Zentralbl. f. Gynäk. 23: 198, 1899. (83) *Keller, R.:* Arch. franco-belges de chir. 33: 568, 1932. (84) *Kelly, H. A.:* Bull. Johns Hopkins Hosp. 7: 29, 1896. (85) *Idem:* 10: 115, 1899. (86) *Idem:* Tr. Am. Gynec. Soc. 31: 225, 1906. (87) *Idem:* 37: 3, 1912. (88) *Kerr, J. M. M.:* Proc. Roy. Soc. Med. 14: 193, 1920/21. (89) *Kleefisch, Johannes:* Zentralbl. f. Gynäk. 54: 258, 1930. (90) *Klumper, P.:* Nederl. tijdschr. v. Geneesk. 2: 674, 1922. (91) *Kolischer, Gustav:* Wien. med. Presse 38: 1630, 1897. (92) *Kolischer, Gustav, and Jones, A. E.:* Urol. & Cutan. Rev. 29: 593, 1925. (93) *Kulenkampf, D.:* Zentralbl. f. Gynäk. 51: 1909, 1927. (94) *Latzko, W.:* Wien. klin. Wchnschr. 44: 103, 1931. (95) *Idem:* Zentralbl. f. Gynäk. 57: 1026, 1933. (96) *Légueu, F.:* Gynécologie 27: 385, 1928. (97) *Idem:* Surg. Gynec. Obst. 48: 796, 1929. (98) *Lower, W. E.:* Tr. Am. Surg. Assn. 48: 336, 1930. (99) *Idem:* J. Urol. 26: 141, 1931. (100) *McGill, A. F.:* Lancet 2: 966, 1890. (101) *McGlinn, J. A.:* Am. J. Obst. & Gynec. 24: 262, 1932. (102) *Mackenrodt, A.:* Zentralbl. f. Gynäk.

18: 180, 1894. (103) *Idem:* Monatschr. f. Geburtsh. u. Gynäk. **5:** 445, 1897. (104) *Madden, T. M.:* M. Press & Circ. **43:** 545, 1887. (105) *Mandelstamm, Al.:* Zentralbl. f. Gynäk. **56:** 334, 1932. (106) *Mann, M. D.:* Internat. M. Mag. **2:** 547, 1893/94. (107) *Marion:* An. de Fac. de med., Montevideo **4:** 765, 1919. (108) *Martin, A.:* Ztschr. f. Geburtsh. u. Gynäk. **19:** 394, 1890. (109) *Martius, H.:* Ztschr. f. Geburtsh. u. Gynäk. **103:** 22, 1932. (110) *Mayo, C. H.:* Ann. Surg. **63:** 106, 1916. (111) *Mayo, C. H., and Walters, W.:* Surg. Clin. N. A. **4:** 399, 1924. (112) *Meriel, E.:* Gynécologie **27:** 467, 1928. (113) *Miller, C. J.:* New Orleans M. & S. J. **82:** 850, 1929/30. (114) *Müller, G.:* Časop. lék. česk. p. 1357, 1925. (115) *Naegeli, T.:* Deutsche Ztschr. f. Chir. **200:** 445, 1927. (116) *Neugebauer, F. L.:* Arch. f. Gynäk. **33:** 270, 1888; **34:** 143, 1889; **35:** 257, 1889; **39:** 508, 1891. (117) *Nicodemi, Cesare:* Riforma med. **2:** 73, 1898. (118) *Noble, C. P.:* Am. J. Obst. & Gynec. **13:** 395, 1898. (119) *Ottow, B.:* Zentralbl. f. Gynäk. **51:** 349, 1927. (120) *Idem:* **53:** 1444, 1929. (121) *Paine, H. S.:* Albany M. Ann. **9:** 65, 1888. (122) *Parvin, Theophilus:* M. Rec. **1:** 321, 1866. (123) *Peterson, Anders:* Am. J. Surg. **17:** 247, 1932. (124) *Phaneuf, L. E.:* Am. J. Surg. **19:** 29, 1933. (125) *Rawls, R. M.:* Curtis' Obstetrics and Gynecology **3:** Chapter LXXXII, Philadelphia, 1933, W. B. Saunders Co. (126) *Richard:* Bull. et mém. Soc. de chir. de Paris **26:** 258, 1900. (127) *Roeder, C. A.:* Surg. Gynec. Obst. **45:** 102, 1927. (128) *Rübsamen, W.:* Arch. f. klin. Chir. **118:** 220, 1921. (129) *Routier, M.:* Bull. et mém. Soc. de chir. de Paris **23:** 90, 1897. (130) *Ryan, Michael:* London Med. J. **6:** No. 144, 1834. (131) *Samter, O.:* Zentralbl. f. Chir. **59:** 1734, 1932. (132) *Schauta, F.:* Monatschr. f. Gynäk. **1:** 8, 1895. (133) *Schroeder, E.:* Monatschr. f. Geburtsh. u. Gynäk. **23:** 60 and 129, 1922. (134) *Scudder, Ida:* Tr. Seventh Cong. Far East Assn. Trop. Med. **1:** 355, 1927. (135) *Sears, N. P.:* Am. J. Obst. & Gynec. **18:** 267, 1929. (136) *Seitz, L.:* Arch. f. Gynäk. **142:** 74, 1930. (137) *Simon, Gustav:* Monatschr. f. Gynäk. **12:** 42, 1858. (138) *Idem:* Operation der Blasenscheidenfisteln, Rostock, Stiller's Hofbuchhandlung, 1862. (139) *Idem:* Am. J. Obst. & Gynec **2:** 232, 1869. (140) *Sims, H. M.:* New York J. Gynec. **3:** 415, 1893. (141) *Sims, J. M.:* Am. J. M. Sc. **23:** 59, 1852. (142) *Spencer, R.:* Tr. Am. Gynec. Soc. **50:** 110, 1925. (143) *Straunch, P.:* Cor.-Bl. D. allg. ärztl. Ver. v. Thüringen **20:** 137, 1891. (144) *Suchon, Edmund:* New Orleans M. & S. J. **15:** 194, 1887/88. (145) *Tait, Lawson:* Dublin J. M. Sc. **85:** 381, 1888. (146) *Trendelenberg, Friedrich:* Samml. Klin. Vortr., No. 355, 1890. (147) *Trombetta, Francesco:* Gior. internat. d. sc. med. **5:** 829, 1883. (148) *Turenne, Augusto:* Assoc. Med. Arg. Rev. **29:** 95, 1918. (149) *Vance, R. A.:* Cleveland M. Gaz. **3:** 135 and 175, 1888. (150) *Vitrac:* Gaz. hebd. **4:** 1190, 1899. (151) *Vogt, E.:* Zentralbl. f. Gynäk. **56:** 1105, 1932. (152) *Ward, G. J.:* Surg. Gynec. Obst. **25:** 126, 1917. (153) *Watkins, T. J.:* Surg. Gynec. Obst. **40:** 274, 1925. (154) *Webb, M. V.:* Tr. Seventh Cong. Far East. Assn. Trop. Med. **1:** 351, 1927. (155) *von Winckel:* Ztschr. f. Geburtsh. u. Gynäk. **30:** 463, 1894. (156) *Wilkerson, T. B.:* N. Car. M. J. **12:** 315, 1883. (157) *Wisniewski, F. F.:* Ill. M. S. **51:** 483, 1927. (158) *Wützer, C. W.:* Org. f. d. ges. Heilk. **2:** 469, 1842. (159) *Idem:* Deutsche Klin. **1:** 32 and 43, 1849. (160) *Young, H. H.:* Surg. Gynec. Obst. **45:** 226, 1927. (161) *Zangemeister, W.:* Zentralbl. f. Gynäk. **53:** 352, 1929.

Bagetti, Mario: Lipoma of the Fallopian Tube, La Ginecologia **2:** 211, 1935.

Emphasizing that primary benign tumors of the fallopian tubes are not uncommon, the author describes a case of lipoma of the tube, found in a thirty-eight-year-old woman during an operation.

Lipoma of the fallopian tubes is rare. More importance is attached to the anatomicopathologic interest than the clinical. This newgrowth represents an accidental finding during a surgical intervention or at autopsy. The growth has no specific symptomatology.

August F. Daro.

TUBAL REIMPLANTATION—IN RETROSPECT*

GEORGE DE TARNOWSKY, M.D., F.A.C.S., CHICAGO, ILL.
(From the University of Illinois School of Medicine and Ravenswood Hospital)

IN JUNE, 1934, L. E. Burch published an article on sterilization of the female in which he made the statement that "there is no absolute surgical method of producing sterilization in 100 per cent of cases." It is my desire to challenge this statement and to present, for the second time before this society, a method called tubal reimplantation which I devised in 1911. Four desiderata were uppermost in my mind in devising this procedure:

1. It must be uniformly successful
2. It must not interfere with the physiologic function of the oviducts
3. It must not unsex the women, i.e., neither ovulation nor libido should be interfered with
4. It must be susceptible of reconstruction, i.e., the continuity of both fallopian tubes to the uterine cavity should be capable of restoration

The first three postulates have been completely attained. No intra- or extrauterine pregnancies have supervened; no case of hydrosalpinx has occurred in any of the sixty cases which form the basis of my report and, finally, ovulation and libido have remained normal. To date none of these patients has evinced any desire to court pregnancy; no attempt at reconstruction of the severed tubes has been possible.

In addition to the four principal desiderata, the operation should be a comparatively simple one, carrying with it, per se, no danger to life nor serious incidence of morbidity, and the approach to the tubes should be such as to enable the surgeon to correct any intra-abdominal lesions which might be present.

Twenty-four years ago, when contraceptive methods were hesitatingly suggested by our profession, the *raison d'être* for sterilization was narrowly restricted. Chronic cardiac lesions, active tuberculosis, nephritis, diabetes, and hereditary insanity usually covered the list of nondebatable indications. DeLee taught that any disease which was a contraindication to pregnancy was an indication for sterilization. Curtis[22] lays down the following conventional postulates for sterilization:

1. All those indications for therapeutic abortion which are based upon prolonged or permanent pathologic conditions
2. Repeated hyperemesis gravidarum in the same patient

*Read at a meeting of the Chicago Gynecological Society, May 17, 1935.

3. Chronic renal disease
4. Permanent cardiac lesions with decompression
5. Repeated cesarean section
6. Active tuberculosis
7. Dementia precox
8. Uterine prolapse requiring the interposition operation or ventrofixation
9. Eugenic sterilization

We are in full agreement with all of these indications.

When tubal reimplantation was discussed before the Chicago Gynecological Society in 1913 four cases were reported. Two of the patients had active tuberculosis, the third was a multipara suffering from chronic nephritis who developed eclampsia at the time of her last parturition, and the fourth a multipara who, following a ventral suspension for prolapsus, became pregnant. She developed such marked pelvic disturbances that intervention was suggested and accepted. The adhesions encountered were so dense and extensive that it was deemed best to sterilize the patient and empty the uterus.

No sterilizations should be performed on unmarried girls unless marriage is contemplated in spite of clearly demonstrable contraindications to pregnancy. With Burch, I believe that sterilization should not be carried out unless contraceptive measures have failed, create esthetic disgust in the mind of one or both partners, or where both parties will not cooperate in their use. Vasectomy is accepted by a few husbands, strongly objected to by many.

In this present day and age, with the joint consent of both husband and wife, tubal sterilization can and should be offered in lieu of contraceptives or mathematical attempts to determine the so-called "safe period." Both are open to the unquestioned objection that they are not infallible and that they tend to destroy the romance of union. This statement is made in all seriousness and should not be misconstrued. Question either husband or wife sympathetically and tactfully; one will be much enlightened by their expressions of regret or disgust that cohabitation should have become such a prearranged and mechanicochemical procedure.

The almost innumerable methods of female sterilization may conveniently be grouped as follows:

1. Mutilating operations:
   - Hysterectomy
   - Bilateral ovariectomy
   - Bilateral salpingectomy
2. Crushing and ligation of tubes (Madlener, etc.)
3. Tubal knotting (Flatau)
4. Electrocoagulation of the isthmial portion of the tubes
   - Vaginouterine route (Dickinson, Hyams, etc.)
   - Abdominal route (Scheffzek)

5. Plastic operations on the tubes:
   - On the uterine end of the tube
   - On the fimbriated end of the tube
   - Broad ligament infolding of the tube
6. Vaginal route (Heaney, Falls, etc.)
   - Crushing and ligation
   - Partial or complete salpingectomy
7. Incarceration of both ovaries in broad ligament pockets.

The fallopian tubes may be considered to represent the excretory ducts of the ovaries. That the tubes are lined by both columnar and ciliated epithelium continuous with the uterine mucosa; that mucous membranes secrete and excrete, and that there is a more or less constant directing action of the tubal current produced in the peritoneal fluid by the movements of the cilia on the tubal fimbriae, especially on the fimbria ovarica, is of common knowledge. There is some difference of opinion as to the relative importance of tubal peristalsis and ciliary movement, probably both are equally concerned. The important point to stress is that the oviducts are secreting tubes requiring an outlet yet, so far as one can determine from close perusal of the literature, only two of the many operations described provide for uninterrupted tubal drainage, namely the one devised by Carey Culbertson[7] and by me. Culbertson, attacking the problem from the distal end of both tubes, makes stab wounds in the broad ligament through which he draws the fimbriated ends of the tubes, anchoring them to the anterior culdesac. By suspending the uterus in anteversion and suturing the broad ligament to the parietal peritoneum he completely shuts off the fimbriated ends of both tubes from the pelvic cavity. Physiologic drainage of the tubes is not interfered with. When N. Sproat Heaney, at a recent meeting of the Chicago Gynecological Society, was describing the occurrence of a tubal prolapse following vaginal hysterectomy, it was interesting to have him state that there was a profuse watery discharge from the prolapsed tube into the vagina.

Vignes and Barron,[21] in an experimental study on the regeneration of resected and ligated tubes, reported the constant formation of an aseptic hydrosalpinx which distended the tubes and perhaps aided in their regeneration. It would seem logical to infer that reported failures of the Madlener procedure might be explained on the same basis. Culbertson makes the pertinent statement that "in all operations which permanently close the distal stumps of the tubes the possibility of hydrosalpinx must be considered."

Aldridge[3] used a method somewhat similar in principle to that of Culbertson but, instead of shutting off the anterior culdesac from the rest of the pelvic cavity he made a pocket between the peritoneal folds of the broad ligament and sutured the fimbriated ends of both tubes in these pockets. He reports one case in which the patient, five years after sterilization, requested a freeing of her tubes. This was followed by pregnancy and delivery.

Section and ligation of the tubes, closure of the cornua and burial of the distal stumps in pockets have been carried out by many pelvic surgeons.

Slemons[4] excises the proximal ends of both tubes and implants them in the uterine muscle. A stab wound is made 1 cm. deep either on the anterior or posterior wall of the uterus; the severed ends of both tubes are buried in these pockets and sutured in place. The uterotubal angle is closed in the usual manner. No tubal drainage is possible in this type of operation.

Jackson[25] slits the serosa from the uterine cornua outward for a distance of 4 cm., picks up the denuded portion of tube, and resects the denuded portion, ligating both ends. The broad ligament is whipped over the intervening space with a running whip stitch of linen. His object is to interpose 4 cm. of scar tissue between the ligated stumps. Again, no drainage is provided for the distal portion of the tubes.

Scheffzek[5] destroys the interstitial portion of the tubes as well as their lateral portion. Through a Pfannenstiel incision the abdomen is opened, the tubes are severed transversely at their uterine junction. A thin electric needle is then introduced into the lumen of the tubes and their interstitial portions destroyed down into the uerine cavity. The needle is then introduced into the lateral portion of the tubes and the entire canal is destroyed. There can be little doubt regarding the efficacy of Scheffzek's method. The fact that this method of sterilization was used on insane women may account for its destructive thoroughness. A double salpingectomy would seem to be a much simpler procedure.

Burial of the severed and ligated distal stumps in the broad ligament or in the inguinal canal as practiced by Crossen, Irving, and others may provide for a certain amount of drainage if the ligature is digested before scar tissue closes the tube.

Tubal knotting, practiced by Flatau, jeopardizes the circulation of the tubes and should be unreservedly condemned.

Burial of both ovaries in pockets prepared on the anterior or posterior surfaces of the broad ligament result, in a certain percentage of cases, either in the occurrence of a persistent fistula at the point where the ovarian pedicle enters the broad ligament pocket, or if the sutures around the pedicles are too tight, ovarian atrophy, and amenorrhea result.

The Dickinson and Hyams[6] cauterization provides no tubal drainage unless a reverse peristalsis is established; furthermore, the method is uncertain in its results. Hyams states that "in an occasional case it may be necessary to repeat the procedure. After one month the end-result is determined by transuterine insufflation or uterosalpingography. Distortion of the uterine cavity by fibroids may render electrocoagulation of the tubes difficult or impossible."

Naujocks[8] proposed a "reversible" (temporary) sterilization of the female by crushing the fallopian tubes. He crushes both ampullas for a distance of at least 1 cm., care being taken to include both muscle and mucosa. One must be sure, he states, that, although the tube is crushed, it is not cut or torn. It is then doubly ligated at each end of the crushed area with some nonabsorbable material. The method is advantageous because it is quick, simple, and bloodless, and because it is easily reversible at a late date by simply cutting the tube between the proximal ligature and the uterus, either with a knife or an endotherm cautery. To date Naujocks has no reported any "reversals." Theoretically, one must admit the probability of sloughing of the crushed and ligated fimbriated ends occurring, with restoration of tubal patency.

Rubovits and Kobak[9] recently reported two failures of the Madlener technic. Fuchs[10] examined twelve Madlener types of sterilization and found five of them to be failures anatomically and functionally. Wolff reported that eight of his Madlener operations were functional failures because the lipiodol passed the point of crushing and was visualized up to the fimbriated ends of the tubes.

The vaginal route, advocated by Falls, Heaney, and others, usually involves complete peritonization of the distal stump of both tubes, either against the anterior wall of the uterus or by bringing the round and broad ligaments over the stumps and uterine cornua wounds at the same time, thus peritonizing the entire field of operation. Tubal drainage is not provided for.

Rosenberg[19] reports a case of left tubal pregnancy six months after performing a modified Pomeroy sterilization. Through an anterior colporrhaphy he ligated and resected a large loop of the cornual ends of both tubes and followed this by electrocoagulation of the severed ends of the tubes. His case, and other similar ones, would seem to prove that, unless tubal drainage is directed away from the cornua, failures will occur.

As illustrating the extremes to which gynecologists have been put in attempting to elaborate a uniformly successful method of sterilization, one may mention, en passant, the method of Zomakion, Haendly and Polan which involves the plastic construction of a double vagina, the anterior, smaller tube for menstruation and cervical drainage, the larger, posterior one for coitus.

Equally fantastic is Baskin's[22] temporary sterilization by the injection of human spermatozoa. From 2 to 5 c.c. of semen to which has been added 1 c.c. of hexylresorcinol is injected in the wife's buttock. Three injections, one week apart, are given. One week after the last injection the woman's serum is tested and similar tests are run every three months. Baskin claims a sterilization of one year's duration following this technic.

The steps of the tubal reimplantation as originally described,[1] are as follows (Figs 1, 2, and 3):

1. Through a four-inch-long paramedian incision the pelvic cavity is opened, its contents inspected and any subacute or chronic changes, including the appendix, are attended to primarily.

2. The fundus uteri is grasped with vulsellum forceps and drawn up through the incision.

3. Amputate the tubes one-fourth inch from the cornua. With a fine rat-tooth forceps or a probe, invaginate the cornual stumps and close the lumen with two catgut sutures. Seroserous coaptation must be complete and firm. It will be occasionally necessary to use a portion of uterine wall to complete the cornual invagination.

4. On the posterior uterine wall and close to its fundus make two parallel vertical incisions one inch long and one-half inch apart. These incisions should not be over one-fourth to one-fifth of an inch deep. With a curved forceps gently burrow between the two parallel incisions, thus creating a canal of sufficient size to contain both tubes.

5. With the same curved forceps remaining in the canal, grasp the opposite tube and draw it through the canal so that it emerges on the opposite side; reverse the forceps and repeat the same procedure with the remaining tube. In the new canal the tubes should parallel each other, one lying above the other, the cut extremity of each tube emerging on the opposite side of the canal.

6. Make a small cuff by everting the tubal mucosa (it is sometimes necessary to make two small incisions before being able to evert satisfactorily) and secure the

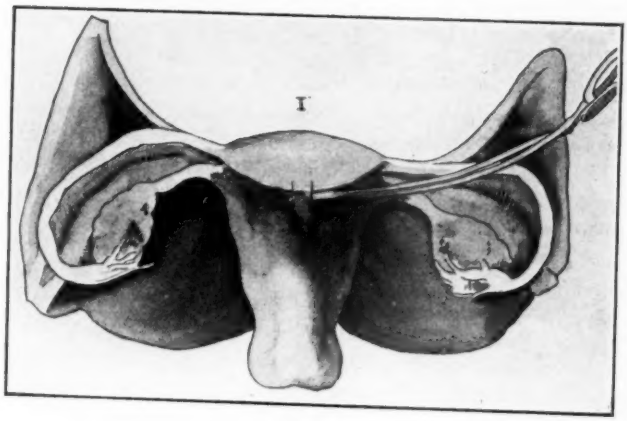

Fig 1.

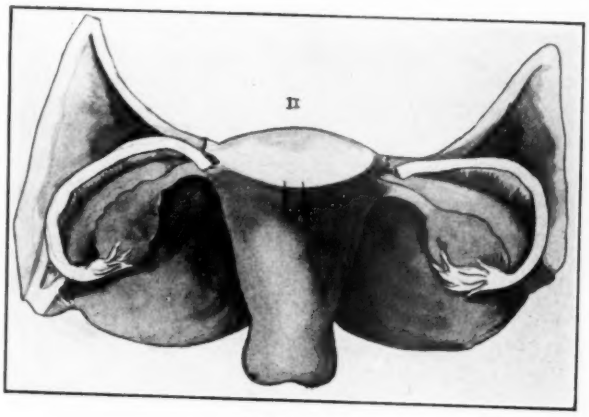

Fig. 2.

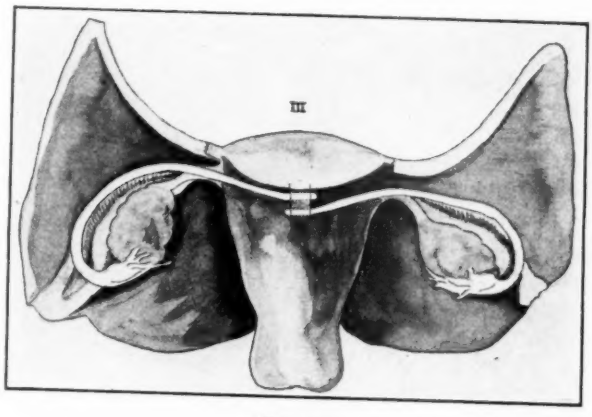

Fig. 3.

cuffs to the margin of the canal by fine catgut sutures which at the same time control any uterine wall oozing which may be present. Test the patency of both tubes by means of a fine probe.

7. Close the abdominal incision in the usual manner.

The only modification in the original technic consists in omitting eversion of the distal ends of the reimplanted tubes. By simply applying two fine catgut stitches uniting each tubal end to the slit or canal in the posterior wall of the uterus, the mucosa is seen to roll outwardly thus preventing tubal closure by adhesions. Where the tubes are unusually small in caliber, a circular portion of uterine wall is included in the cornual excision. This makes a rosette-like stump which is easier to suture in place. There is ample clinical evidence that these tubes remain patent and that the tubal ciliated epithelium continues to function normally. Repeated examinations of sterilized patients have failed to reveal any tubal enlargements. That the ovaries of these patients continue to function normally up to the average climacteric age is amply proved by the follow-up of sixty private patients:

POSTOPERATIVE MENSTRUAL HISTORY

DURATION OF MENSTRUATION	NO. OF CASES OBSERVED
10 years	14
9 years	16
8 years	5
7 years	8
5 years	6
4 years	8
2 years	3
Total	60

Discreet and tactful questioning regarding libido following sterilization warrants the statement that it is unchanged in 25 per cent and decidedly increased in 75 per cent of these cases. The increased libido must be ascribed to the removal of fear of pregnancy. Patients report a definite improvement in sex life following sterilization.

As previously stated, no actual proof of the possibility of restoration of the continuity of the tubes can be offered. Should occasion arise, reconstruction ought to be possible. The invaginated portion of the uterine stumps could be resected, the distal ends removed from their artificial uterine canal and an end-to-end anastomosis obtained with very fine interrupted catgut sutures. This could be done either vaginally or abdominally.

There should be, and, so far, has been no mortality from the tubal reimplantation which has been used, as occasion demanded, for some twenty-two years. Analysis of the sixty follow-up cases has been extremely gratifying:

Mortality		None
Morbidity		5%
	Omental adhesions 1	
	Dysmenorrhea 2	
Psychic disturbances		None
Surgical amenorrhea		None
Libido	Unchanged 25%; Increased 75%	

SUMMARY

1. A simple, safe and, so far, uniformly successful method of tubal sterilization is reviewed, sixty cases being analyzed as to morbidity and end-results.

2. The operation should never be undertaken in the presence of any acute abdominopelvic infection, but subacute or chronic pathologic conditions can be removed at the same time without increasing the incidence of mortality or morbidity.

3. The principle of the operation is based on the belief that preservation of tubal excretion prevents the possible formation of an aseptic hydrosalpinx.

4. Ovarian function is not disturbed.

5. On theoretical grounds the operation can be used as a temporary means of sterilization.

REFERENCES

(1) *Tarnowsky, G. de:* Tubal Reimplantation, J. A. M. A. **60:** 893, 1913. (2) *Bush, L. E.:* Am. J. Surg. **24:** 3, 1934. (3) *Aldridge, A. H.:* Am. J. Obst. & Gynec. **27:** 741, 1934. (4) *Slemons, J. M.:* Am. J. Obst. & Gynec. **27:** 775, 1934. (5) *Scheffzek, F. A.:* Zentralbl. f. Gynäk. **58:** 2786, 1934. (6) *Hyams, M. N.:* Am. J. Obst. & Gynec. **28:** 96, 1934. (7) *Culbertson, C.:* Surgery of the Female Pelvis, New York, 1923, D. Appleton-Century Co., p. 319. (8) *Naujocks, H.:* Zentralbl. f. Gynäk. **55:** 81, 1931. (9) *Rubovits, W. H., and Kobak, A. J.:* Am. J. Obst. & Gynec. **27:** 12, 1934. (10) *Fuchs, H., and Lork, E. C.:* Montaschr. Geburtsh. u. Gynäk. **88:** 199, 1931. (11) *Walz, W.:* Zentralbl. f. Gynäk. **56:** 2007, 1932. (12) *Madlener, M. M.:* Zentralbl. f. Gynäk. **56:** 2731, 1932. (13) *Malcrieff:* Gynec. et obst. **25:** 217, 1932. (14) *Granella, C.:* Zentralbl. f. Gynäk. **57:** 938, 1933. (15) *Kulenkrampff, D.:* Deutsche med. Wchnschr. **59:** 1294, 1933. (16) *Chamarro, J. A.:* Semana méd. **2:** 449, 1933. (17) *Zocchi, S.:* Boll. d. soc. piemontese di ost. & ginec. **1:** 198, 1933. (18) *Saenger:* Arch. f. Gynäk. **156:** 157, 1933. (19) *Rosenberg, M.:* Am. J. Obst. & Gynec. **24:** 154, 1932. (20) *Zomakion, A.:* Zentralbl. f. Gynäk. **49:** 2404 1925. (21) *Vignes, H., and Barron, F.:* Bull. Soc. d'obst. et de gynéc. **4:** 225, 1931. (22) *Baskin, M. J.:* Am. J. Obst. & Gynec. **24:** 892, 1932. (23) *Curtis, A. H.:* Obst. & Gynec. **111:** 224, 1933. (24) *Turenne, A.:* Surg. Gynec. Obst. **29:** 577, 1919. (25) *Jackson, G. B.:* J. A. M. A. **99:** 2026, 1932.

30 North Michigan Avenue

Ghosh, Sudhangsu Kumar: An Unusual Case of Traumatic Haemorrhage From the Vagina, Calcutta M. J. **29:** 173, 1934.

The author reports a case of rupture of posterior wall and fornix of vagina during intercourse, in a multipara, aged twenty-six, causing profuse hemorrhage. Patient was confined six months previously and had had puerperal fever for several weeks.

It was the first coitus after delivery, followed by free blood discharge. Examination showed a lacerated wound in posterior vaginal wall longitudinally from 1 inch above introitus to posterior fornix, 2½ inches by 1 inch and muscle deep. No scar tissue was seen in vagina. Sutures had to be passed through fascial layers.

Fatal coitus injuries are on record. After prolonged illness the soft attenuated vagina yields easily to small pressure. In this multipara, the vaginal tissue was possibly abnormally soft.

F. L. Adair and S. A. Pearl.

HEMATOMETRA*

JOHN A. MCGLINN, M.D., F.A.C.S., AND
W. BENSON HARER, M.D., F.A.C.S., PHILADELPHIA, PA.
(From the Departments of Gynecology of the St. Agnes Hospital and Fitzgerald Mercy Hospital)

HEMATOMETRA is a condition that has received but scant attention in recent medical literature. Even in such a comprehensive work on obstetrics and gynecology as the new Curtis textbook, we find it referred to only in connection with congenital malformations of the genital tract and then in a very incomplete form. Reference on this subject in recent years has been limited practically to simple case reports, owing probably to the relative rarity of the condition. However, hematometra is undoubtedly becoming more frequent and this fact, together with certain points of unusual interest in two of our recent cases, prompts us to present this report.

No definite statement can be made concerning the incidence of hematometra. The condition is so rare that many gynecologists of broad experience have never encountered a case. In certain countries, however, the condition is becoming more common. Thus, in Russia in eighteen months prior to January, 1927, twenty cases of hematometra occurred in one series of 1,500 cases of induced abortion as a result of atresia of the cervix due to improper curettage.

Etiologically, hematometra is always the result of an occlusion of the genital tract at some point external to the uterine cavity. This occlusion may be either congenital or acquired and may be either a complete occlusion of the genital tract or, more rarely, may at first be only a partial occlusion. The congenital cases are due to malformations of the genital organs, such as imperforate hymen, absence of vagina, uterus duplex unicollis with no cervical opening, double vagina in which one canal is blind, etc. Such cases at times constitute most difficult gynecologic problems but fortunately are quite rare. The more commonly encountered cases are those due to an acquired atresia of the lower genital tract. In such cases the occlusion frequently is the result of overzealous curettage of the uterus and especially of the cervical canal, improper cauterization of the cervix from the use of too heavy a cautery tip, or the application of caustics to the cervix. The increasingly frequent application of radium to the cervix and uterine cavity in the treatment of cervical or fundal carcinoma and of menorrhagia or metrorrhagia due to other causes is

*Read at meeting of the Obstetrical Society of Philadelphia May 2, 1935.

resulting in an ever increasing incidence of cervical atresia. This usually follows the use of improperly screened radium by relatively inexperienced operators. Another etiologic factor in the production of an acquired hematometra is adhesions of the cervical canal or vagina resulting from infections of the birth canal. One of our cases, in which the vaginal atresia was the result of a gonococcal infection, well illustrates this point, but is unusual in that such occlusions are quite uncommon as a sequel of gonorrhea. Still another etiologic factor that should be stressed today is atresia of the vagina resulting from improper use of the Elliott treatment of pelvic inflammatory conditions. Although of undoubted value, this treatment is not without danger; especially when, as is frequently the case, its application is entrusted to a nurse or office attendant. Recently, a number of cases of severe burns of the vagina, several with complete atresia, have been reported following such treatments.

The signs and symptoms of hematometra depend somewhat upon the site of the genital occlusion and whether this occlusion is partial or complete. If partial, the patient complains of severe dysmenorrhea and greatly prolonged menses with the passage of black, tarry material. This recurs for a variable number of times, generally with progressively increasing severity until eventually the occlusion of the genital tract becomes complete, after which the lower abdominal pains, backache, headache, general malaise, etc., continue to recur but with no accompanying vaginal discharge. If the site of occlusion is in the lower part of the vagina, the pain becomes marked in this region and swelling of the vulva with bulging of the perineum much like that seen in labor appears. Later on, prominence of the lower abdomen develops and on palpation a rounded mass closely resembling a pregnant uterus may be felt. If the condition is allowed to proceed still further, the tubes then become distended and may be felt as large, tender, fluctuating, sausage-shaped masses in the pelvis or lower abdomen. If the fimbriated end of the tube remains patulous, these masses slowly decrease in size in the intermenstrual period and may even return practically to normal size. Such a discharge of menstrual fluid into the abdominal cavity gives rise to all the signs and symptoms of a chemical type of peritonitis and eventually results in the production of an endometriosis.

These signs and symptoms first appear at puberty in all congenital and in some acquired cases of hematometra. In such cases, when the occlusion of the genital tract is complete there is a history of complete amenorrhea together with the signs and symptoms just described. In those acquired cases, occurring later in life, there is a history of normal menstruation up to the time of occurrence of the condition or opera-

tion which produced the genital atresia, after which there is amenorrhea and the development of the above described symptoms.

The pathology of hematometra is quite interesting. If the site of occlusion is near the vulva, the vagina, because of the elasticity of the walls, first balloons out with the menstrual fluid, resulting in the development of hematocolpos. The uterine muscle at first becomes greatly hypertrophied as a result of the efforts made to expel the menstrual blood. Accompanying this muscular hypertrophy we have marked thickening of the endometrium. Eventually the accumulation of blood in the vagina reaches the stage of maximum distensibility of the vaginal tissues and then the uterus begins to distend and hematometra results. The increasing intrauterine pressure causes atrophy of both the endometrium and uterine muscle. This endometrial atrophy tends to somewhat lessen the quantity of menstrual blood produced during each period and so somewhat retards the further development of the condition. However, in time, the menstrual fluid is squeezed out into the fallopian tubes, distending them and then spilling out into the peritoneal cavity. The abdominal spill sets up a chemical type of peritonitis with the usual result of formation of dense adhesions particularly in the culdesac and to the posterior uterine wall. Since viable endometrial cells are frequently present in the menstrual discharge, these cells may lodge on the ovary due to its close proximity to the end of the tube and so give rise to ovarian endometriosis. Finally, as a result of the prolonged irritation by the menstrual blood and the formation of adhesions, the tubes become sealed off at the abdominal end. From this time on there is only continued distention of all affected parts and marked increase in symptoms until treatment is given or rupture occurs.

Time and space do not permit a full discussion of the differential diagnosis of hematometra. Among the commoner conditions which hematometra may simulate may be mentioned the delayed onset of the menses at puberty, pregnancy with threatened abortion, acute appendicitis, relaxation of the sacro-iliac joints, pelvic inflammatory disease, peritonitis, and endometriosis. A careful history and thorough physical examination should suffice to differentiate these conditions in most cases.

The treatment of hematometra depends upon the duration and the cause of the condition. In cases occurring at puberty where the condition is recognized before hematosalpinx has developed, simple vaginal drainage secured by incision of the occluding membrane or lysis of adhesions, is all that is required. The surgical correction of any congenital abnormality of the genital tract is, of course, indicated. In neglected cases, vaginal drainage is contraindicated because of the danger of subsequent peritonitis from ascending infection of the genital tract. All neglected cases and most acquired cases of hemato-

metra occurring later in life are best treated by laparotomy and removal of all pathologic tissue. Occasionally, conservative treatment by vaginal drainage may be employed in acquired cases occurring later in life.

CASE REPORTS

CASE 1.—Mrs. M. B., aged forty-five, para ii, last child nine years ago. Chief complaints: Backache and severe pain in lower abdomen. Patient was perfectly well until after the birth of her first child, twelve years ago, then began to suffer with profuse and prolonged menstrual periods. She was treated without much relief and finally was advised to become pregnant again in the hope that another pregnancy might clear up this condition. She followed this advice, but with the resumption of the menstrual function following the birth of her second child, the menorrhagia again returned. Six years ago radium was inserted in the uterus to control the uterine bleeding. Following this she had no vaginal bleeding at any time. She was then well until about two years ago when she began to suffer with severe pain in the back, in the lumbosacral region. This pain began abruptly and continued for five days, during which time she first consulted one of us (W. B. H.). Examination at that time failed to reveal any definite cause for the pain and the condition cleared up under symptomatic treatment. About three months later she suffered a similar attack, which again cleared up after about seven days. The patient was then not seen until about nine months later when she returned, complaining of pain in the back and severe cramplike pains in the lower abdomen. She stated at this time that the attack of pain had come on about two weeks previously and this time had lasted for about nine days. She further stated that she had been thoroughly studied in one of the large hospitals of Philadelphia for a period of six weeks and had been told that she had visceroptosis, a severe secondary anemia and a floating tumor the size of an orange in the region of the left fallopian tube. Examination at the time of this visit revealed no evidence of such a tumor even though the patient was examined in both the reclining and erect positions. Following this visit the patient was again lost sight of until March, 1934, when I was called to see her at her home. At this time she was suffering with very severe pain in the lower abdomen which had started the previous day. Examination at this time revealed rigidity and marked tenderness over the entire lower abdomen. Before a vaginal examination could be done, the patient then volunteered the information that in the interval since I had last seen her she had had a similar attack during the acute stage of which she had been examined by another gynecologist who told her that she had fibroids and strongly urged that she undergo a course of x-ray treatments for this condition. Vaginal examination at this time revealed a symmetrically enlarged, hard, tender uterus and a soft cystic mass about the size of a small grapefruit in the left adnexal region. I told the patient that I agreed with the diagnosis of fibroids but that she also had an ovarian cyst and that therefore she should be operated upon rather than treated with x-rays. The next day she again called me and agreed to go to the hospital. After carrying out the usual preliminary work, the patient was given 90 mg. of avertin per kilo of body weight. An attempt was made to do a preliminary dilatation and curettage but no opening could be found in the cervix. The true diagnosis was then apparent and laparotomy was immediately performed. The uterus was symmetrically enlarged about the size of a four months' pregnancy. The right tube and ovary were bound down into the culdesac with dense adhesions. This tube was greatly distended and sausage-shaped. The left tube was greatly enlarged, black in color and black tarry blood was oozing from the fimbriated end of the tube. The left ovary contained a large chocolate cyst. The entire pelvic organs were bound down to the sigmoid, small intestines and omentum by dense adhesions. After free-

ing these adhesions supravaginal hysterectomy with bilateral salpingo-oophorectomy and appendectomy was performed. The abdomen was closed without drainage and the patient made an uneventful recovery. The pathologic diagnosis was hematometra due to cervical atresia, bilateral hematosalpinx and chocolate cyst of the left ovary. The patient has been entirely free of symptoms ever since.

CASE 2.—A. K., aged twelve. First seen July 10, 1929. Gave history that she had been under treatment for three years for gonorrheal vulvovaginitis. Treated locally with antiseptics, local cleanliness, various dyes and autogenous vaccines. Seen again on Jan. 18, 1934, at which time she was twelve years of age. Examination showed growth of hair on pudenda and increased size of breasts. Menstruation, however, had not been established. Four days before her visit, she had severe pains in her lower abdomen and two days later had a fever of 102° for one day. When seen on January 18, she still had pain. There was no vomiting, no abdominal rigidity; bowels had moved with enema. She was not tender over appendix and had normal peristalsis. There was some faint pigmentation of the linea alba.

Rectal examination made but was not satisfactory due to the resistance of the patient. We found a mass, apparently the uterus, which was hard and large. Her parents were advised to take her to the hospital for examination under anesthesia, but the child refused and the parents gave in to her whim. The pains subsided and she apparently recovered from her attack. On Feb. 12, 1934, she was again taken with severe pains in her abdomen and I was asked to see her at her home. The recurrence of the pains approximately twenty-eight days after her first attack made me feel sure it was due to menstruation. I refused to accept the call as no examination could be made at the home and I again urged the parents to bring her to a hospital. Not until four days later was this done. On February 16, a rectal examination under gas revealed the uterus enlarged to about the size of a three months' pregnancy. The vaginal orifice was virginal, and I felt satisfied we were dealing with retained menstrual blood in the uterus. Vaginal examination showed the upper part of the vagina walled off by adhesions so that the cervix could not be reached. These adhesions, while dense, were easily broken up and the cervix exposed. With the breaking up of these adhesions a large amount of tarry blood escaped from the uterus.

The diagnosis was hematometra due to retained menstrual blood back of vaginal adhesions, the result of gonorrheal infection of vagina.

Note: At no time had any caustic applications been used in the vagina.

CASE 3.—The patient (Miss B. G.) was one week overdue on her menstrual period. Believing herself to be pregnant she consulted a physician with the object of having an abortion performed. Some form of electrical apparatus was used in the vagina in an attempt to induce abortion. The result was a severe burn of the vault of the vagina, but no abortion. Several weeks later she was seized with severe backache, headache, and cramplike pains in the lower abdomen. This lasted for five days and gradually disappeared. About a month later the same condition occurred. Three months later, after three more such attacks, she consulted one of us (J. McG.). Abdominal examination revealed a rounded, tender mass, about the size of a four months' pregnancy in the lower abdomen. On vaginal examination dense adhesions were found in the upper part of the vagina, completely occluding the vagina, so that the cervix could not be felt. Because of the absence of other signs and symptoms of pregnancy, and the fact that the uterus was smaller than would be expected from the history, it was felt that pregnancy could be ruled out. A diagnosis of hematometra was made and laparotomy was performed. The uterus, both tubes, and one ovary were removed. The pathologic report was hematometra.

SUMMARY

Hematometra is an accumulation of menstrual blood within the uterine cavity due to either a congenital or an acquired atresia of the lower genital tract.

Increasingly frequent and improper uterine curettage, improper application of radium to the cervix, the use of caustics and heavy cautery tips in cervical cauterization, and the improper application of the Elliott treatment of pelvic infections are stressed as important factors in the increasing frequency of acquired hematometra.

The signs and symptoms and the pathology of hematometra are discussed. Vaginal drainage of early cases and radical treatment by abdominal hysterectomy of neglected cases and those occurring later in life, are advised.

Three cases of acquired hematometra are reported.

REFERENCES

Kraul, L.: Ztschr. f. Geburtsh. u. Gynäk. **106:** 64, 1933. *VanLuyn, W. L.:* Nederl. tijdschr. v. geneesk. **77:** 3362, 1933. *Lifvendahl, R. A.:* Am. J. Obst. & Gynec. **26:** 173, 1933. *Lefebvre:* Bull. Soc. d'obst. et de gynéc. **22:** 728, 1933. *Gal, F.:* Gyógyászat **73:** 357, 1933. *Villaca, O.:* Rev. de gynec. e d'obst. **27:** 302, 1933. *Valentini, A. Landauro, and Villamon, F.:* H. Rev. Med. pernano **5:** 757, 1933. *Porter, H. K.:* M. J. Australia **1:** 496, 1933. *Bizard, G., and Lambret, M.:* Arch. franco-belges de chir. **33:** 783, 1932. *Worrall, R.:* M. J. Australia **2:** 751, 1932. *Martins, P.:* Gynéc. et. obst. **27:** 152, 1933. *Mazel, M. S.:* Illinois M. J. **62:** 84, 1932. *Pla, F. Terrades:* Mundo med. **14:** 597, 1932. *Allain-Conti:* Rev. gén. de clin. et de thérap. **46:** 343, 1932. *Graham, I., and Anderson, C.:* M. J. Australia **2:** 178, 1932. *Borras, P. E.:* Rev. med. latino-am. **17:** 852, 1932. *Mouradian, A. H.:* M. J. & Rec. **135:** 369, 1932. *Snodgrass, M. R.:* J. A. M. A. **97:** 777, 1931. *Rao, S. S.:* Brit. M. J. **1:** 180, 1931. *Klaften, E.:* Zentralbl. f. Gynäk. **55:** 1257, 1931. *Vikoulof, A. V.:* Gynéc. et. obst. **21:** 500, 1930. *Calverley, J. E. G., and Buttery, J. W. D.:* Brit. M. J. **1:** 590, 1930. *Grant, W. H., and Rose, D.:* Am. J. Obst. & Gynec. **19:** 555, 1930. *Gogoberidze, B. K.:* Odessky M. T. **2:** 23, 1927. *Vikuloff, A. V.:* J. akush. i. zhensk. boliez. **40:** 514, 1929. *Genell, S.:* Acta obst. et gynec. Scandinav. **8:** 177, 1929. *Gutierrez, A.:* Rev. de cir. **7:** 369, 1928. *Drips, D. G.:* M. Clin. North America **12:** 1577, 1929. *Areta, T.:* Semana med. **1:** 930, 1928. *Areta, T.:* Semana med. **2:** 237, 1928. *Iribarne, T., and Contreras Ortiz, N.:* Rev. de cir. **7:** 93, 1928. *Simon, H. E.:* Surg. Gynec. Obst. **47:** 356, 1928. *Vignali, A.:* Clin. obst. **30:** 86, 1928. *Gouillioud:* Lyon chir. **24:** 484, 1927. *Cox, H. H., and Bougher, A. H.:* Illinois M. J. **49:** 43, 1926. *Curtis, A. H.:* Obstetrics and Gynecology **3:** Philadelphia, W. B. Saunders Co., p. 672. *Bass, A.:* Zentralbl. f. Gynäk. 1927.

1900 Rittenhouse Square

Bak, M.: The Value of Finger Prints in Twins, Monatschr. f. Geburtsh. u. Gynäk. **99:** 271, 1935.

At the Budapest Midwife School, Bak studied the finger prints of twins. He failed to find identity in the finger prints of either single ovum or double ovum twins. There was, however, a similarity between the prints, most marked in single ovum twins. The author believes that this similarity may be used for medicolegal purposes.

J. P. Greenhill.

A CONSIDERATION OF THE PHENOMENON OF OVULATION AND ITS RELATION TO THE SEX CYCLE*

IRVING F. STEIN, B.S., M.D., F.A.C.S., CHICAGO, ILL.
(From Northwestern University Medical School and Michael Reese Hospital)

THE phenomenon of ovulation is fundamental to the reproductive process, but our knowledge concerning the exact time of occurrence of this phenomenon in the human being, the mechanism thereof, and its relation to the associated changes in the sex cycle is still far from complete. Our understanding of the endocrine stimulation of ovulation is just beginning to dawn, and the relationship between ovulation, corpus luteum formation, and menstruation is being acknowledged. The analogy of the sex cycle in the human being to that of lower mammals inclines one to accept certain facts revealed by animal experimentation and to apply them directly, but one outstanding observation tends to cast doubt upon such analogies, namely, that the function of menstruation is to be observed in the primates alone. The great variation which exists in the gestation periods in mammals, from twelve or thirteen days in the opossum to nearly two years in the elephant, suggests that there may also be great discrepancies in the fecundity of ova and spermatozoa as well as in the conditions for mating. In lower animals, mating is usually restricted to a few hours or days before ovulation, while in primates there is no set rule. While in all mammals one observes certain similarities in pattern, there are also differences both in the structure and the function of many organs. The human organism stands out as being unique, and as Beaumarchais so aptly said, "Drinking without being thirsty, and making love at all seasons distinguishes man from beasts." In some of the smaller mammals, copulation stimulates ovulation. This is true according to Allen, in the cat, rabbit, and ferret; in others, spontaneous ovulation is the rule. In primates, ovulation is probably spontaneous, yet it is not definitely known whether in certain females the stimulation of coitus may not induce multiple ovulation and follicle rupture at variable times in the cycle. According to the most recent opinion (Ball and Hartman), ovulation is not ascertainable with accuracy in women at the present time. The pituitary extract test of Knaus, though a valuable one for experimentation, is not applicable clinically. Frank's hormone test, though an excellent one, must be simplified for practical usage.

With a view to stimulating further thought upon this fundamental question, I desire to present what data I have been able to assemble in

*Presidential Address before the meeting of the Chicago Gynecological Society, June 7, 1935.

as simple a form as possible. I have very little that is original to offer; merely the kernels which I have gathered from the sources which were available to me.

EVIDENCE OF OVULATION TIME IN WOMEN

L. Fraenkel was the first to show that ovulation precedes menstruation. From evidence obtained by the examination of the ovaries at operation, he concluded that ovulation occurred on the eighteenth day of the cycle. Schroeder from a study of operative material also placed ovulation at the fourteenth to sixteenth day in regular four-week cycles, and Meyer and Ruge stated it to be on the eighth day or during menstruation itself, and later (Ruge, 1919) concluded that ovulation occurred on the eighth to the fourteenth day in the cycle.

Ogino placed ovulation on the twelfth to sixteenth day before the onset of the next menstruation (after examining 118 women at laparotomy), and Knaus concluded from his work that in women with normal reproductive physiology, ovulation always takes place on the fifteenth day before the onset of menstruation.

Asdell, after a study of 568 cases in which operative and autopsy material was used, stated that the period of ovulation is variable in the menstrual cycle, occurring most frequently between the eighth and seventeenth days.

Additional evidence of the time of ovulation is presented by Allen, Pratt, Newell and Bland by obtaining 5 young human ova at operation. Of their 40 observed patients, 26 operations were performed between the twelfth and sixteenth days of the cycle. The ova obtained by tubal washing were found, 1 on the fourteenth, 3 on the fifteenth, and 1 on the sixteenth days. They concluded from the condition of the ova when found that ovulation occurred in these women between the twelfth and fourteenth days after the first appearance of the previous menses. Lewis recovered one ovum on the eighteenth day after a previous cycle of thirty-five days and Hyrtl found one in the interstitial portion of the tube on the fourth day (DeLee). In this connection, Swezy comments that when the number of tubal eggs found is compared with the number of cases examined during the middle of the cycle, with not only *no evidence* of ovulation, but with the uterus and ovary in the anestrous or resting phase, it is strong evidence that this test is inadequate. He considers the *amount of proliferation* of the endometrium to be the criterion upon which to judge ovulation time.

From data obtained by measuring the size of graafian follicles, Allen and Papanicolaou concluded that ovulation might occur anywhere from the second to the twenty-eighth day of the cycle. From another angle, Teacher tabulated time of fertilization and embedding of the ovum estimated from the study of early ova as reported by various authors. As may be seen (Table I), fertilization was estimated to have occurred throughout most of the cycle, from the sixth to the twenty-eighth day, and embedding from the thirteenth to the twenty-eighth day of the current cycle and through the fourth day of the succeeding one. In addition, Triepel estimated the ovulation time from observations upon early embryos and found it to be the eighteenth or nineteenth day of the cycle; Grosser on the second to the twenty-fourth day, and Volkmann, fourth to the twenty-fifth day (Table II).

Frank studied the quantitative anterior pituitary-like hormone and blood estrin throughout the cycle along with the urinary estrin excretion. He found an acute rise in anterior pituitary up to the time of follicle ripening, followed by a gradual fall to zero just before menstruation. At the same time, the blood estrin rose

acutely after ovulation to reach its height at the onset of menstruation, followed by a rapid drop during the period. Meanwhile the urinary estrin increased irregularly, reaching a peak about three days before menstruation.

TABLE I. ESTIMATED TIME OF FERTILIZATION AND EMBEDDING FROM STUDY OF EARLY OVA (TEACHER)

FERTILIZATION	DAY OF CYCLE	EMBEDDING
Merttens	6	
Rossi Doria	7	
Bencke	8	
Eternod	13	Merttens
	14	Rossi Doria
	15	Bencke
Peters	16	
Jung	17	
Von Spee (Glavecke)	19	
Von Spee (Von Herff)	21	Eternod
Frassi	23	Peters
Teacher, Bryce, and Reichert	24	Jung
Leopold	25	
	26	Von Spee (Glavecke)
	28	Von Spee (Von Herff)
	After menses	
	2	Frassi
	3	Teacher, Bryce, and Reichert
	4	Leopold

TABLE II. ESTIMATED TIME OF OVULATION FROM THE STUDY OF EARLY EMBRYOS

Triepel	18th or 19th day
Grosser	2nd to 24th day
Volkmann	4th to 25th day

Knaus claims to have determined the exact time of ovulation by ascertaining the extent to which the human uterus loses its sensitiveness to posterior pituitary extract, in the presence of the corpus luteum hormone. This test requires the placing of a balloon into the uterus and of making manometric tracings on a kymograph. In women with a twenty-eight-day cycle, the uterus reacts with spontaneous rhythmic contractions in the first fourteen days and responds to pituitary stimulation. The capacity of the uterine cavity is 3 or 4 c.c. in the first two weeks, but on the sixteenth day increases to 8 to 10 c.c., is flaccid, and shows almost no spontaneous contractions. Now, it no longer responds to pituitary stimulation until the twenty-ninth day or twenty-four hours before menstruation, when it resumes the activity of the first half of the cycle.

Knaus believes that this test may be used as an accurate gauge of ovulation time, corpus luteum secretion causing abolition of spontaneous uterine contractions and rendering the uterus unresponsive to pituitary extract.

Particular significance is placed upon evidence obtained from the study of the reproductive cycle in the monkey, which, in some respects at least, is comparable to that in the human being. Thus, Ivy states, "In monkey and man it is generally agreed, and I consider it proved, that 'spontaneous' ovulation occurs about the middle of the twenty-seven- or twenty-eight-day cycle." On the other hand, Allen says that while in the monkey ovulation occurs on the thirteenth or fourteenth day, and in some cases as early as the tenth or eleventh day, that the ovulation time in primates may vary beyond these limits in irregular cycles, and that mating stimuli might possibly induce ovulation at other times. Fertile coitus in the monkey ranged from the ninth to the eighteenth days in the sixty cases observed by Hartman.

The discovery of a reliable and practical clinical test for ovulation appears to be near at hand, but is not as yet within our grasp. There is much that requires elucidation.

LIFE OF THE OVUM

The exact endocrine "hook-up" responsible for follicle development and ovulation is not as yet definitely known, but is at present assumed to be a reciprocal relationship between the hormones from the ovary and the anterior lobe of the pituitary gland. In the rabbit the actual process of ovulation has been observed, the rupture of the follicle occurring slowly, accompanied by a flow of thick, viscid, blood-tinged fluid. In the human being, the follicular fluid is thin and under considerable pressure, so that the actual mechanism of rupture may not occur in just the same manner, but may be more precipitous. Midmonth pain, when it occurs, but by no means the rule, is probably caused by rupture of the mature graafian follicle. After rupture, the ovum, free in the peritoneal cavity, finds its way into the fimbriated end of the fallopian tube. The mechanism of transit from the ovary to the tube, whether by chemotaxis, by suction set up by the ciliary wave, or enzyme action, is not understood as yet. More definite knowledge is at hand, however, concerning life of the mammalian ovum (Table III).

TABLE III. LIFE OF THE OVUM (IVY)

	HOURS	DAYS	EVIDENCE
Rabbit	4-5		Certain
Opossum	24		Certain
Mouse	24		Certain
Sow	24		Certain
Dog		5-6	Not certain
Human	48		Not certain

According to Knaus, the unfertilized human ovum has a very short life, possibly less than twelve hours. Degenerative changes, he states, set in within a few hours after extrusion and a laminated layer of follicular cells, the corona radiata, surrounds the ovum. These follicular cells are soon shed and an albuminous sheath which is supposedly derived from the tubal epithelium forms about the ovum. This sheath is impenetrable to spermatozoa, thus limiting the period of fertility to a few hours after extrusion from the follicle. This view presupposes that one and only one ovum is available for fertilization during each cycle. On the other hand, in the laboratory of Dr. Otto Saphir, I have observed sections of the human ovary with the three maturing follicles near the surface of the cortex, each containing an ovum which might possibly be extruded on different days of the same cycle (Fig. 1). Stockard and Evans have both suggested the probability of extracyclic ovulation.

It is furthermore generally held that the presence of the corpus luteum inhibits further ovulation, and that a single corpus luteum is to be

found in the ovary during the last two weeks of each cycle. Exceptionally, I have seen two recent corpora lutea at slightly different stages

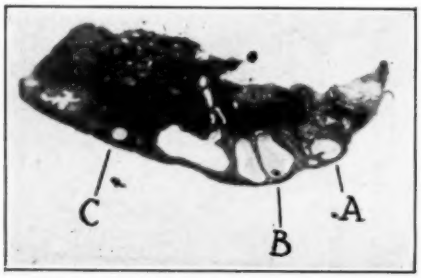

Fig. 1.—Section of human ovary with three maturing graafian follicles.

Fig. 2.—Left, high power of *A* and *B* shown in Fig. 1. Right, higher power of *A*, showing ovum.

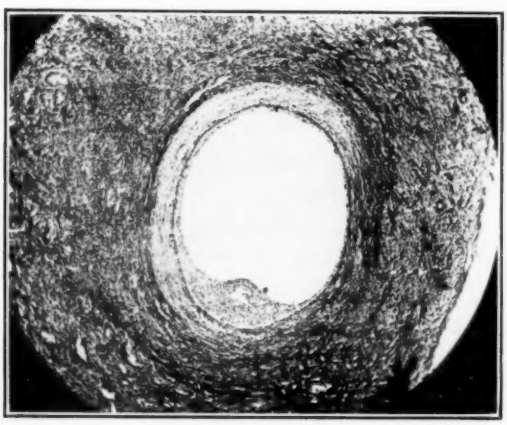

Fig. 3.—High power of *C* shown in Fig. 1.

of development in the section of an ovary which indicated the maturation of two ova in the current cycle. These observations tend to throw

considerable doubt upon the sterility-fertility rhythm theory as propounded by Knaus and Ogino, dependent as it is upon a single ovum at a fixed time in the cycle.

LIFE AND FECUNDITY OF SPERMATOZOA

More than twenty years ago, Hoehne and Behne stated that human spermatozoa cannot remain fertile in the fallopian tubes longer than three days. The sperms probably reach the fimbriated end of the tube and the peritoneal cavity within a few hours after coitus, but according to Dührssen and Nürnberger may live in the infundibulum of the tube for at least three weeks. Many authors believe, however, that the fertilizing power of the sperms is short, probably not more than three days. Knaus says it is less than two days, and this holds for the spermatozoa of all mammals with scrotal testes; that the intraabdominal temperature plus the alkaline secretion of the fallopian tubes tend to limit their

TABLE IV. LIFE OF SPERMATOZOA (KNAUS)

	HOURS
Rabbit	30-48
Rat	12-16
Guinea pig	41
Pig	41½
Horse	48
Bat	Several months (all winter)
Human	48 (or less)

fecundity. Spermatozoa kept at body temperature in vitro remain fertile for about sixteen hours, and at the freezing point for about seventy-two hours. They remain fertile longer at room temperature than in the incubator, and longer in the vagina of a dead animal than one alive. Knaus believes that the life of the human spermatozoa in the uterus and tubes is considerably shorter than in animals. He says that the overabundance of sperms which are provided at coitus is an absolute necessity for fertilization, for only a few can survive the powerful defense works of the mucosa of the female generative tract. He also states that this defense is less powerful at the time of ovulation.

It appears to me to be unreasonable to ascribe to the generative organs a quality of defense, placing great obstacles in the way of the male germ cells when the prime function of those organs is reproduction. Does nature intend that reproduction be made intricate and difficult, or is the mechanism set up for safety and protection of the male and female egg?

CONCEPTION LIMITATIONS

Knaus and Ogino independently have determined that ovulation occurs regularly on the fifteenth or sixteenth day, before the appearance of the succeeding menstruation. They are agreed that the fertile period is

limited to approximately three days before and two days following ovulation. They have accumulated considerable clinical data to substantiate their claims. Furthermore, Miller, following the fertility-sterility rhythm of Knaus and Ogino, reported on 126 couples who held intercourse 1,429 times in the "sterile" portion of the month without the occurrence of a single conception, and 49 instances of coitus between the twelfth and nineteenth days of the cycle resulting in conception.

On the other hand, Dickinson assembled a mass of evidence from various sources from which he adduced that: (1) Conception can occur at any part of the month. (2) There is a very marked difference between favorable and unfavorable periods (72 per cent in the first two weeks, about 7 per cent in the premenstrual or "sterile" week, and 13 per cent during menstruation). He also showed that the days of the month of maximum sex desire and maximum well-being occurred simultaneously at the time of *minimum* chance for conception, namely, in the premenstrual week. This would indicate that woman by nature is led to cohabit most frequently when chances for pregnancy were low, or, according to Ogino and Knaus, *were nil*. By comparison with the monkey, this is indeed inconsistent, for most recent studies indicate (Ball and Hartman) that sex desire in the monkey reaches its height just *prior to ovulation*, and that the premenstrual rise which occurs in women is entirely absent.

One can hardly ignore the accumulated data of conceptions occurring in women with twenty-eight-day cycles and resulting from single acts of coitus; 1,342 cases were assembled by Dickinson in which no days of the month were exempt; most conceptions occurred after coitus on the sixth, seventh, and eighth days, 72 per cent in the first two weeks, about 13 per cent during the menses, and from 7 to 10 per cent in the fourth week of the cycle. Fraenkel, on a recent visit to this country, expressed an opinion which entirely coincides with that published by Dickinson. His personal series of almost 200 cases of isolated coitus showed about the same proportions of conceptions distributed similarly in the cycle as those quoted above, and he concluded that there is no regular safe period for women. Furthermore, he emphasized that a minimum of women menstruate regularly every twenty-eight days.

COMMENT

There is a growing literature encompassing valuable data concerning the phenomenon of ovulation and its relation to the sex cycle. As yet, we have no practical clinical test for ovulation nor do we entirely comprehend the detailed mechanism of follicle rupture and tubal entrance. As a matter of fact, we must admit that, although we have amassed much information, we possess very few facts. We are intrigued by the theory of a fertility-sterility rhythm in women and we look forward eagerly to the next decade of carefully collected clinical data concerning its application. If nature has provided a definite safe period before the

twelfth day and after the ninteenth day of the regular twenty-eight-day cycle, it is indeed contrary to the principle of perpetuation of the species to place the period of maximum sex-desire and euphoria exactly in the sterile phases of the sex cycle. There is a discrepancy somewhere, and it becomes the task of the clinician and physiologist to jointly weld the chain of facts.

In closing, I would urge physicians to collect accurate data concerning the exact menstrual cycle in their patients, and note such facts as time of intercourse, midmonth pain, and sex desire. The calendar method appears at present to be adequate for literate women. If such data would be assembled, then in a few years we would, in all likelihood, be enabled to answer some of the perplexing questions concerning human reproduction.

REFERENCES

(1) *Allen, E.:* Sex and Internal Secretions, Baltimore, 1932, Williams & Wilkins Company. (2) *Allen, Pratt, Newell, and Bland:* Am. J. Anat. **46:** 1, 1930. (3) *Ball and Hartman:* Am. J. Obst. & Gynec. **29:** 117, 1935. (4) *Corner, G. N.:* Carn. Inst. Cont. Embryol. **13:** 117, 1921; **15:** 73, 1923. (5) *Davis, K. B.:* Factors in the Sex Life of 2,200 Women, New York, 1929, Harper & Brothers. (6) *DeLee, J. B.:* Principles and Practice of Obstetrics, ed. 5, Philadelphia, 1929, W. B. Saunders Co. (7) *Dickinson, R. L.:* Am. J. Obst. & Gynec. **14:** 718, 1927. (8) *Evans, E., and Swezy, O.:* Am. J. Physiol. **96:** 628, 1931. (9) *Frank, R. T.:* J. A. M. A. **103:** 394, 1934. (10) *Hartman, C.:* Science, p. 226, 1931. (11) *Ivy, A. C.:* Notes on Ovulation. (12) *Knaus, H.:* Periodic Fertility and Sterility in Woman, Vienna, 1934. (13) *Novak, E.:* Menstruation and Its Disorders, Monographs, New York, 1931, D. Appleton-Century Co. (14) *Ogino, K.:* Conception Period of Women, Harrisburg, Pa., 1934. (15) *Saphir, Otto:* Personal communication. (16) *Swezy, O.:* Am. J. Obst. & Gynec. **29:** 246, 1935.

310 South Michigan Avenue

Gasquet, P.: The Treatment of Pruritus Vulvae by Infiltration With Radon in the Pruritic Area, Rev. franç. de gynéc. et d'obst. **29:** 1079, 1934.

In many cases of pruritus vulvae, local treatment is of no avail. The subcutaneous injection of novocaine solution has only a temporary effect. Radiotherapy is followed by certain accidents. Resection of the presacral nerve requires an operation. Gasquet applied radon or the emanation of radium externally but the results were not entirely satisfactory. He, therefore, resorted to the subcutaneous injection of radon into the area of pruritus. He gives daily injections and sometimes only three a week of between 400 and 800 millimicrocuries of radon. The injection is never painful. The relief sometimes manifests itself after the first injection but more often after the third. The author has never had to give more than 15 injections. The action of the radon is on the terminal nerve endings from where, because of its affinity for nerve tissue, the radon ascends as high as the nerve trunks, thereby producing a sedative action upon the territory inervated by these nerves. The treatment is entirely innocuous as proved by the total disintegration of the radon within about a month after it is administered. This holds true regardless of the dose injected.

J. P. Greenhill.

A CLINICAL TEST OF THE NEWLY RECOGNIZED OXYTOCIC PRINCIPLE OF ERGOT AND A NEW METHOD OF ADMINISTRATION

VERNON L. TUCK, M.D., SHERMAN, TEXAS

CONSIDERABLE has been said in the recent medical literature with reference to a previously unrecognized oxytocic principle of ergot and the manner in which it proves its superiority over the older preparations in initiating uterine contractions. At the time of this writing it seems well established that a pure crystalline substance has been isolated by Thompson,[1] and Dudley and Moir[2] from ergot, of definitely alkaloidal nature, which gives rather startlingly splendid results when used in various ways as an oxytocic. The results would indicate that the two groups working separately have been successful in isolating the same alkaloid. Another article[3] calls attention to the fact that the Baltimore worker no doubt was the first to appreciate the true alkaloidal character of the product. Thompson has given the name ergostetrine and the English group have utilized the term ergometrine for their respective alkaloids. At about the same time, in this country, a Chicago group, Davis, Adair et al.[4] reported the isolation of a non-alkaloidal fraction of ergot which they have produced in crystalline form, that seems to possess the same degree of activity as attributed to the acknowledged alkaloidal crystals of the other workers. Dudley and Moir[3] object for obvious reasons to the name ergotocin given to this third product since it was applied originally to a more crude extract rather than to the purified crystalline form. Regardless of the name of the ergot derivative, however, and the priority of claim, all three are apparently superior to any other ergot preparation previously used. None of these workers attempted a method of administration which has proved in this clinical series more adequate than any other in quickness of action, ease of administration and consistency of results, namely, by rectum. However, Jones and Barlow[5] believe that the older ergot preparations give a more satisfactory result by this route.

The method of study in this series obviously differs from the procedure followed by the other investigators, since the object was to give the alkaloid a thorough clinical trial on the postpartum uterus and to form some ideas concerning its adequacy in controlling postpartum hemorrhage, maintaining good uterine tone during the early puerperium, the consistency of its actions by various routes of ad-

ministration, and the possibility of decreasing the incidence of morbidity by shortening the duration of the so-called normal period of lochia rubra and by hastening involution. These are in large the questions that interest the obstetric profession. Whereas the other investigators used the uterine bag and abdominal tambour methods of study, our method consisting of manual palpation of the fundus uteri and clinical observation may at a casual glance seem rather crude; however, it has proved quite satisfactory in the hands of the accoucheurs these many years. It can be readily understood that more elaborate methods cannot be followed routinely on the wards of a charity hospital where the obstetric turnover is so rapid.*

The drug used in this series was furnished by Dr. M. R. Thompson, of the School of Pharmacy, University of Maryland, through the courtesy of John Wyeth and Brother. For hypodermic use the alkaloid ergostetrine was dissolved into a 20 per cent alcoholic solution standardized to contain 0.5 mg. ergostetrine per 1 c.c. which proved to be the optimum dosage for that mode of administration. However, the drug for oral and rectal use was a product containing 20 per cent alcohol (supplied as ergoklonin) standardized to contain 0.1 mg. ergostetrine per 1 c.c., and proved most satisfactory by both routes in one drachm dosages. All of the women participating in this study were in the third trimester of pregnancy and the drug was used immediately after the second or third stages of labor, as will be shown later. In initiating the study, a series of control cases was run in which our old hospital routine, consisting of U.S.P. ergot after the second stage of labor and one ampule of pituitary solution U.S.P. after the third stage, was carried out, but after running fifty alternate cases in this manner, the results were so promising with the newly recognized alkaloid that the control series was dropped. At no time in the remainder of the series was it necessary to supplement the new drug with any other oxytocic. Among the women delivered in the series there were: Primiparas 105, multiparas 227, episiotomies 61, forceps 23, versions 1, eclampsias 5, positive Kahn 12, breech 12, abruptio placentae 2, twins 2, and stillborn babies 15.

The selection of the most satisfactory mode of administration proved to be one of the most interesting phases of the study. The drug was given by mouth in the early cases and proved itself adequate. The one drachm dose, 0.4 mg. of ergostetrine, was diluted to 2 ounces with water, largely to assist in its passage rapidly through the pyloric sphincter of the stomach into the small bowel where it is rapidly absorbed. It is thought that absorption takes place more rapidly than

*This series of cases was studied on the Obstetrical Wards of the Philadelphia General Hospital through the courtesy of the following chiefs: Drs. John A. McGlinn, Harry A. Duncan, and Clifford B. Lull.

with the other ergot alkaloids due to the smaller size of the new alkaloid molecule. It seems almost unnecessary to add that a stomach distended with food tends to slow the passage of the drug into the small gut, and hence delays the onset of its oxytocic action. Irregardless of how the new oxytocic drug was given at the time of delivery, it was given orally in the one drachm dose diluted with two ounces of water three times daily on the first three postpartum days, as is routine on most obstetric services. The hypodermic route was used in some of the patients delivered under general anesthesia and offers no variation from the technic generally employed. Suffice it to say that to date no irritations or infections have resulted from its usage.

The rectal route, however, surpassed all expectations in offering a method of administering this drug. In retrospect, one wonders why a drug so commonly used in obstetrics over such a long period of time, as ergot, has not been given a thorough trial by the rectal route, especially when the anal dimple occupies such a central position in the field of a delivery. The ease of injection, speed of reaction and efficacy of uterine contractions require that this route be considered more in detail. A rubber catheter, size 18-21, has proved most satisfactory as a means of introducing the solution into the rectum. The catheter, lubricated with green soap or any other similar medium, is advanced three to four inches from the anus into the rectum or to any point inside the internal sphincter. While the tube is held in place the one drachm dose is diluted with two to three drachms of water and either forced through the catheter with a syringe or allowed to flow through by gravity after using a small funnel as a reservoir. Care should be taken to withdraw the tube slowly after injection, and it seems advantageous to have the tube clamped off with the fingers while pulling through the sphincter. In only one condition has it been necessary to insert the tube higher into the rectum and that is when the patient is so deeply anesthetized that there is complete relaxation of the anal sphincter. In this case, by introducing the catheter to about eight inches and allowing it to remain for one and one-half minutes after injection of the drug, followed by a slow withdrawal, all danger of leakage is obviated and in that time sufficient of the drug has been absorbed to give an entirely satisfactory oxytocic effect on the uterus. One other factor probably has been of definite advantage in avoiding a premature spill from the rectum. It has been given routinely only after expression of the placenta in order to avoid being expressed by massage of the fundus as is routine in some clinics. By observing these precautions, all danger of leakage is avoided and the mode of administration is certainly more simple and efficient than any we have previously tried.

The type of uterine contraction resulting from the use of the new alkaloid is characteristically different from that given by pituitary solution. Rather than giving a tonic spasm to the uterine musculature, it gives a clonic effect with very firm contractions lasting one and one-half to two minutes and followed by a mild degree of relaxation, but not sufficient to cause complete loss of tonus, as proved on kymographic tracings by a failure of the curve to return completely to the base line between contractions. Following the short interval of relative relaxation usually lasting about one minute, the cycle of contraction and relaxation is repeated over a period of several hours, showing a gradual decrease both in the tendency to return toward the base line during the periods between contractions and in the frequency of remissions or relaxations, thus leaving the uterus in a more or less contractile status. Irregardless of the method of administration, the uterine reponse has been consistently of this type and leaves no doubt in the mind of anyone palpating the fundus uteri as to the adequacy of contraction as well as to the absolute cessation of bleeding from the uterus.

At the present time, although the work has not been completed, 184 patients have been delivered, in whom only oral administration has been utilized. In the large majority of these the drug was given following the second stage of labor and at no time has there been a placenta retained in utero for longer than thirty minutes and in several instances the placenta was expressed into the vagina by the oxytocic alone. The onset of contractions was noted in these cases by the palpating fingers in three minutes as the shortest time and six minutes as the longest, the variation probably resulting from failure of passage of the drug into the small bowel in the more refractory ones. In studying the U.S.P. fluid extracts of various drug houses, the shortest time in which any of them worked orally was twelve minutes, and that with a variable response. This oral route was used chiefly in multiparous women who required only analgesia for delivery.

The hypodermic route was used in only twenty deliveries due to the splendid results from the rectal administration and our desire to give the latter route a thorough clinical trial. The contractions always resulted after hypodermic injection in from two to four and one-half minutes, being slightly more rapid in onset than after oral administration, but in no way giving a better result. Most of these patients were under general anesthesia and the administration whether after the second or third stage seems to be merely a matter of the obstetrician's preference.

At the present time 128 patients have been delivered with the new oxytocic being used only by rectum. The results have been astonishing and the procedure is being recommended, without reservation, to

the attention of the profession in order that it may get a wider clinical trial. In these cases there has been a contractile response on the part of the uterus in one to two and one-half minutes which differs in no particular from that resulting from the oral and hypodermic routes except in the speed with which it affects the uterus. It is of interest to note that a Gwathmey analgesia preceding the ergostetrine has in no instance delayed the latter's action. This is also true of a general anesthesia although the loss of sphincter control makes it necessary to use a little more care in giving the drug by rectum; but as pointed out previously, attention to two or three minor details will obviate the danger of expulsion and of contamination of the operative field. The rectal administration was routinely done after the third stage of labor for a definite reason as previously noted.

It can be positively stated that when the drug is given after the second stage of labor, there is a noticeable decrease in the amount of blood lost during the entire delivery. In addition it is important to note that no cases of even moderately severe postpartum hemorrhage have occurred; but at one time during the study a temporary lack of the newer drug necessitated the use of U.S.P. fluid extract of ergot and pituitary solution for about one week, and during this interval three moderately severe postpartum hemorrhages were encountered, two of them requiring uterine packing. With the new drug there was also a decrease in the oozing of blood from the uterus which is so frequently found for several hours after the patient leaves the delivery room. Ergostetrine administered by any route proved adequate to stop all uterine bleeding within a few moments whether given after the second or third stage of labor.

It is not the purpose of this paper to attempt to express definite opinions concerning the hastening of uterine involution by use of the new oxytocic. However, one is prone to think that there must be many advantages in its use since the lochia is almost free of a bloody tinge after three to four days when the alkaloid has been used in the early puerperium. DerBrucke[6] and many others are of the opinion that shortening the period of lochia rubra hastens involution. It is interesting to note the morbidity incidence in this series. Our morbidity standard is any elevation of temperature above 100° F. occurring twice in twenty-four hours, exclusive of the first twenty-four hours following delivery. The theoretical objection raised by many who have no practical experience with the rectal administration of the oxytocic is that there is imminent danger of its causing infection in the genital tract. This possible danger has not become apparent in this series, probably on account of the care with which the injection is given with our technic. Be that as it may, the morbidity (according to our standard) in 204 patients receiving the drug orally and

hypodermically was 14 per cent. On the other hand, in 128 patients receiving the drug rectally at delivery the morbidity was only 9 per cent. No maternal deaths occurred in this series. It would seem from these results that the rectal route when used properly offers no more danger of infecting the mother than the oral and hypodermic routes.

In summarizing, 332 women, advanced to the third trimester of pregnancy, were delivered using the newly recognized alkaloid as the only oxytocic in the second and third stages of labor. The results were uniformly satisfactory regardless of the mode of administration. No bad results were encountered and the action of the drug indicates that it is far superior to any of the older known oxytocic ingredients of ergot. The splendid response to rectal administration of the drug as evidenced by speed of reaction, consistency of results and ease of administration, makes it necessary to recommend its more widespread use in this manner by various obstetricians and to conclude that the rectal route is the optimum one so far tried.

Sincere thanks must be tendered the resident physicians and obstetrical nursing staff of the Philadelphia General Hospital, without whose able assistance this work would have been impossible.

REFERENCES

(1) *Thompson, M. R.:* J. Am. Pharmaceutical Assn. **24**: 185, 1935. (2) *Dudley, H. W., and Moir, C.:* Brit. M. J. p. 520, 1935. (3) *Dudley, H. W., and Moir, C.:* Science, p. 559, June 7, 1935. (4) *Davis, M. E., Adair, F. L., Rogers, G., Kharasch, M. S., and Legault, R. R.:* AM. J. OBST. & GYNEC. **29**: 155, 1935. (5) *Jones, J. L., and Barlow, O. W.:* AM. J. OBST. & GYNEC. **29**: 489, 1935. (6) *DerBrucke, M. G.:* AM. J. OBST. & GYNEC. **29**: 272, 1935.

Oxley, Phillips and Young: Maternal Mortality in Rochdale—An Achievement in a Black Area, Brit. M. J. **1**: 304, 1935.

Investigation of maternal mortality over a period of six years showed that obstetric factors, frequently preventable, were responsible for the high death rate in that area and not the existing economic ill conditions.

An interest in prophylaxis was stimulated by public propaganda. Antenatal care was increased. Improvement in the obstetric condition followed with a reduction in death rate from 8.9 in 1929 to 2.99 in 1932-34 per 1,000 live births registered.

The standard of maternity service directly affects the end-results. Admitting patients to a hospital early in labor and hospitalization during pregnancy and labor when abnormal conditions prevailed were responsible for better end-results.

By a deliberate effort this community achieved a reduction in its maternal death rate, by a method which may be adopted with success in other centers. This success is due to the mutual cooperation between the public health authority and all those engaged in the maternity services, as well as to the propaganda campaign inspired by the public health department throughout the borough.

The results were obtained by a change of spirit and method, without any alteration in the personnel or any substantial increase in public expenditure. A careful survey is recommended to each administrative area as routine practice.

F. L. ADAIR AND S. A. PEARL.

PRIMARY CARCINOMA OF THE FALLOPIAN TUBE*

With Report of a Case

Walter T. Dannreuther, M.D., New York, N. Y.

(From the Department of Gynecology, New York Post-Graduate Medical School and Hospital, Columbia University)

DAVID N. BARROWS[1] has published a comprehensive paper on primary carcinoma of the fallopian tube in which he reviewed the literature to date, discussed the etiology, symptomatology, and surgical treatment, and reported three cases from the Gynecological Service of Bellevue Hospital, admitted between the years 1911 and 1926. Calling attention to the frequency with which this neoplasm had been observed in the Gynecological Departments of the Johns Hopkins and Bellevue Hospitals, Barrows stated that "it begins to assume a frequency to force our consideration when we are dealing with adnexal conditions." Kahn and Norris[2] subsequently brought the literature further up to date, collecting 270 reported cases and adding four more of their own. Two of these occurred in young married women eighteen years of age, the youngest patients on record. These authors emphasize the apparent increase in the incidence of the disease during the past decade, but attribute this to a more highly "carcinoma-minded" profession and the greater number of excised specimens subjected to microscopic examination. A vivid recollection of Barrows' excellent presentation enabled me to make the correct diagnosis at operation in a recent case. Irregular bleeding from an apparently atrophic uterus and the presence of an obvious unilateral hematosalpinx, in a woman who had passed her menopause fifteen years previously, aroused the suspicion of tubal malignancy. The early diagnosis, miniature development of the lesion (Fig. 1), and complete extirpation of the pelvic organs in this patient encourage the hope that the prognosis is probably better than is usually the case.

CASE REPORT

Mrs. L. B., aged fifty-seven, consulted me on Dec. 2, 1933, complaining of continuous vaginal bleeding for the previous five weeks. Her general health had always been good, and her only prior complaints had been constipation and leucorrhea. Menstruation began at fourteen, and had always been regular and painless. She had been delivered of three full-term babies after hard labors and had one spontaneous abortion. There was no history of pelvic inflammation. Menstruation stopped abruptly at the age of forty-two. Two years later she had one typical menstrual period, and never bled again until just before coming under observation.

*Read before the New York Obstetrical Society, March 12, 1935.

The patient was well nourished but tremendously obese. Except for a blood pressure reading of 178/100, the general physical findings were normal. The portio of the cervix and vaginal fornix were fused in three places by bands of cicatricial tissue, but the cervix was not deeply lacerated or eroded. The uterine corpus was small, retroverted, and almost completely immobilized. The tubes on both sides were thickened and adherent, the one on the left side being distinctly larger. The ovaries could not be identified by palpation.

Operation.—Dec. 6, 1933. When the uterus was curetted, the endometrial surface was found to be atrophic. After opening the abdomen and freeing the pelvis of intestines, the findings on bimanual examination were verified. The left tube was larger than the right, densely adherent, and released with considerable difficulty. It was brownish red in color, clubbed and distended, and obviously contained old blood. A complete hysterectomy, bilateral salpingo-oophorectomy, and appendectomy were done. Convalescence was uneventful until the eighth day, when there was

Fig. 1.—Low power photomicrograph of carcinoma originating in the left fallopian tube.

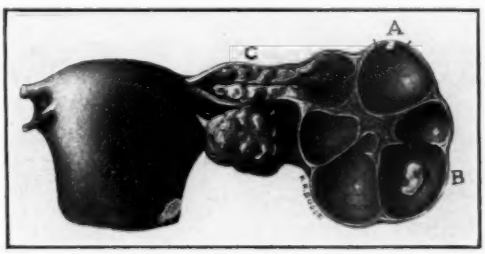

Fig. 2.—Uterus and sectioned left fallopian tube (right adnexa omitted from the drawing). *A*, point or origin of carcinoma; *B*, largest fragment broken off from the primary tumor and lying free in one of the cystlike compartments; *C*, hyperplastic plicae and adherent blood clot at uterine end of the tube. (Semidiagrammatic.)

a dehiscence of the abdominal wound. This was resutured under infiltration anesthesia with through and through silkworm-gut sutures, after replacing three loops of intestine. Secondary union was perfect, and the wound is now well healed without evidence of hernia.

Pathologic Report.—Specimen was a uterus with tubes and ovaries. The uterus measured 35 by 20 by 30 mm. and the myometrium had an average thickness of 16 mm. The tube on the left side was approximately 80 mm. in length and had a proximal diameter of 5 mm. and a distal diameter of 20 mm. The fimbriated end was occluded and the entire tube was distorted and made tortuous by adhesions which bound it to the attached ovary. The ovary on this side measured 30 by 18 by 8 mm. and was markedly fibrotic. On section, the distal portion of the tube consisted of a number of thin-walled cysts containing brownish gray tissue fragments and hemorrhagic fluid (Fig. 2).

The other tube measured 40 mm. in length and had an average diameter of 6 mm. It was firm and cordlike, and the attached ovary measured 25 by 10 by 10 mm. and was equally firm. The fimbriated end of the tube was occluded by adhesions that bound it to the ovary. On section, the tube had a greatly thickened fibrous wall and the lumen was much narrowed. The ovary was buried in dense fibrous tissue.

Appendix was 40 mm. in length and 5 mm. in diameter. On section, the wall was moderately thickened. The lumen, a narrow slit, was filled with brownish material.

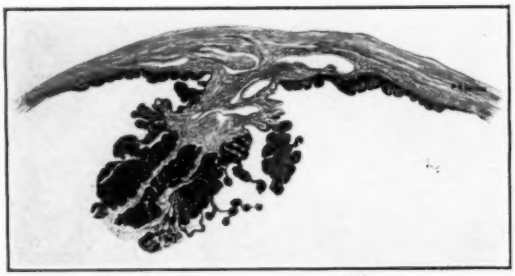

Fig. 3.—Drawing of the papillary excresence, showing coarse convoluted papillae, formed by many layers of deeply stained cuboidal epithelium.

Fig. 4.

Fig. 5.

Fig. 4.—High power photomicrograph, showing anaplastic epithelium with mitotic figures.

Fig. 5.—Drawing of the largest detached fragment, showing structure similar to the atypical epithelium of the tumor attached to the tubal wall.

Microscopic Examination.—Sections of the uterus showed the endometrium lined by scattered epithelial cells, with an underlying layer suffused with blood and serum and infiltrated with lymphocytes and mononuclear cells. This layer was continuous with the stroma of the endometrium, which was scanty and also infiltrated and suffused with blood. The endometrial glands were scattered and rudimentary and were widely separated by the stroma, which was mildly infiltrated by lymphocytes in the deeper part. A few endometrial glands were dilated and were lined by one

or two layers of columnar cells which showed some exfoliation. The myometrium was more densely cellular than usual. The picture denoted curettage.

Sections of the dilated left tube showed a thin wall of fibrous tissue and a partial content of clotted blood, some of which clung to the inner wall. At one point there was papillary thickening with the formation of excrescences composed of deeply staining cells in which there were no lumina (Fig. 3). The epithelium was anaplastic, the cells showed very little cytoplasm, and mitotic figures were numerous (Fig. 4). This is evidently a highly malignant carcinoma, originating from the epithelium of the tube. The pieces of tissue floating in the hemorrhagic fluid exudate filling the dilated portion of the tube showed coarse convoluted papillae formed of many layers of deep-staining cuboidal epithelium. An occasional minute opening in the cell masses suggested tubule formation. The detached fragments showed a structure similar to the papillary excrescence arising from the dilated cystic tube and matched the atypical epithelium of the tumor attached to the tubal wall (Fig. 5). The proximal portion of the tube showed hyperplastic plicae covered by columnar epithelium. The plicae showed much increase in their fibrous stroma, which was mildly infiltrated by lymphocytes and mononuclear cells.

Sections of the other tube resembled the proximal portion of the first tube.

Sections of the left ovary showed corpora albicantia and numerous sclerosed blood vessels, with marked edema and congestion throughout. The tissues of the mesosalpinx in the adherent tube and ovary attachment showed dilated ducts lined by columnar epithelium, several of which showed papillary projections of their lining epithelium, possibly representing remnants of Gartner's ducts.

Sections of the other ovary showed corpora albicantia, numerous sclerosed blood vessels and small cysts with epithelial lining, apparently derived from old graafian follicles.

Sections of the appendix showed fecal material in the lumen, and the mucosa was lined by an intact layer of columnar epithelium. The interglandular stroma was infiltrated by mononuclear cells and occasional eosinophiles. The lymphoid tissue was fairly abundant and edematous, and occasional vessels on the serosal side were surrounded by lymphocytic infiltration.

Pathologic Diagnosis.—Papillary adenocarcinoma of the left fallopian tube, with associated hematosalpinx, chronic salpingitis, and perisalpingitis with adhesions. Chronic salpingitis and perisalpingitis of the right side. Bilateral chronic oophoritis with minute retention cysts. Atrophy of endometrium. Chronic appendicitis.

REFERENCES

(1) *Barrows, David N.:* Am. J. Obst. & Gynec. 13: 719, 1927. (2) *Kahn, Milton E., and Norris, Samuel:* Am. J. Obst. & Gynec. 28: 393, 1934.

580 Park Avenue

Nizza, M.: The Influence of Local Thermo Therapy Upon the Temperature of the Deep Genital Sphere, Boll. d. Soc. piemontese di Ostet. e ginec. 2: 1086, 1934.

Using a thermoelectrical system the author studied the temperature in uterus, vagina, and rectum during the application of cold or heat to the epigastrium. The mean difference in temperatures was 0.26° C. He observed moreover how in some cases the deep temperature of uterus, vagina, and rectum was temporarily lowered by the initial application of heat and raised by cold.

August F. Daro.

MONOAMNIOTIC TWINS, ONE NORMAL, THE OTHER ANENCEPHALIC; MULTIPLE TRUE KNOTS IN THE CORDS*

SOL LITT, M.D., AND HERMAN A. STRAUSS, M.D., CHICAGO, ILL.
(From the Department of Obstetrics, Michael Reese Hospital)

MRS. G. S., a thirty-year-old para iv, entered the Michael Reese Hospital on May 17, 1935, on the service of Dr. R. Gordon. The pains started and membranes ruptured early in the morning of the same day. Her three previous pregnancies had been normal, as had the puerperium except for phlegmasia alba dolens and breast abscess after the third child.

The present pregnancy had been normal until four days before entrance, when fetal movements had no longer been felt and fetal heart tones could not be obtained. The patient would not be at term until June 22, 1935.

The patient entered the hospital at 11:45 A.M. with membranes presenting at the external os. Examination also revealed complete effacement and dilatation of the cervix and a breech presentation, as well as a knotted prolapsed cord. The prolapsed cord was not pulsating. Because of the inability to palpate the cephalic pole of the fetus, the possibility of the fetal deformity was considered. There was also considerable difficulty in outlining the fetal ovoid because the patient was very obese. The diagnosis of intrauterine death of the fetus with possible deformity was made.

At 12:05 P.M. a pulseless cord was visible at the vulva, and at 12:10 a stillborn anencephalic male monster was born by the breech. The cord of this fetus was entangled and knotted with a second cord, and at 12:14 a second stillborn male fetus was born in cephalic presentation. The placenta was expressed at 12:20 P.M., and was complete and intact.

Examination of the specimen revealed a single placenta measuring 15 by 18 by 3 cm. with one chorionic and amniotic sac. The membranes were complete and intact, and there was no evidence of an amniotic partition on the fetal surface of the placenta. Two cords inserted into the fetal surface of the placenta in an eccentric position, and about 2 cm. apart. The cords were free for a considerable distance from the placenta (about 30 cm.) when they were entangled and knotted in multiple true knots. From the knotted area the cords separated again, each then leading to its respective fetus. One fetus was grossly normal in every respect, except for being approximately five weeks premature, and much macerated. The other fetus was a typical anencephalic monster, the cranial vault and contents being entirely absent. A glistening reddish membrane covered the base of the skull. There were no evident abnormalities of the spinal column, or of the rest of the body. The twins were of approximately the same size and stage of development, and there was no evidence of earlier death of either of them. The umbilical cord of the normal twin was wound once around the neck and once around the thorax (not shown in photograph).

COMMENT

This case is of interest because of the relative rarity of a gross developmental anomaly of one twin, the other being normal. The literature makes but little mention of anencephalic and normal twins. DeLee[1] states that the same deformity

*Presented at a meeting of the Chicago Gynecological Society, May 17, 1935.

often occurs in both twins, but does not speak of single deformities in twin births. The more common instances of acardiacus and fetus papyraceus are also noted by this author. Döderlein[2] makes similar remarks on the deformities arising from "asymmetry" in the placental circulation. These cases are, however, due to inequality in blood supply, the one fetus becoming parasitic upon, or compressed by, the other.

A further point of interest is in the multiple knotting of the two cords. It is probable that this knotting, together with the winding of the cord about the neck and body of the normal twin, was responsible for its death. Dietrich[3] has reported a case where entanglement and false knots of the cord tightened after the birth of the first twin, and led to the death of the second before delivery could be effected. It is doubtful that the anencephalic twin was capable of independent existence.

This case represents an instance of monoamniotic twin pregnancy, of which Quigley[4] has recently collected 109 examples from the literature. This author men-

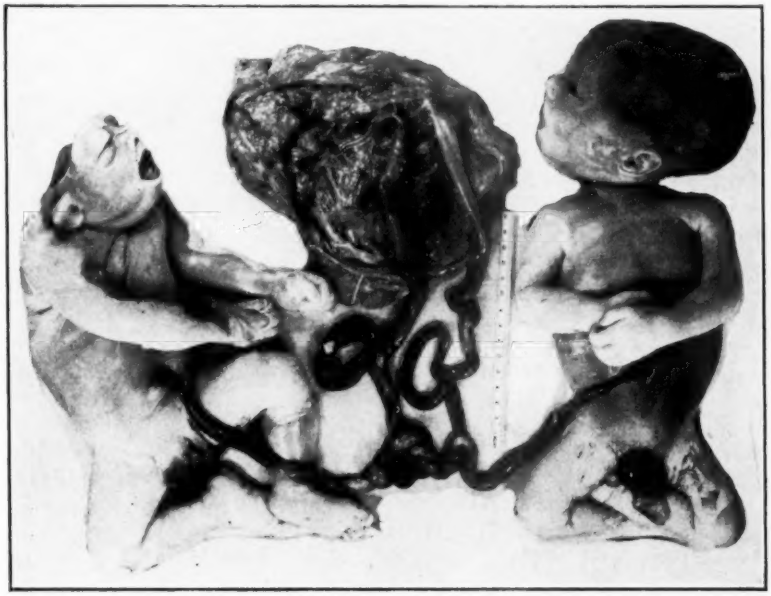

Fig. 1.—Monoamniotic twins, one (left) anencephalic, the other normal. Note multiple knotting of the cords, and absence of amniotic partition between the placental insertions of the cords. Cord of the normal twin was wound once about the neck and once about the thorax.

tioned 8 instances of monsters among the collected cases, but did not describe the types encountered.

There is a possible conformity of this case to the idea of Streeter,[5] that localized deformities in the fetus are due to disparity in the vitality of different tissues of the body. He states that there are found extreme disparities where the tissues have an anomalous excess of vitality and growth potency or in the other direction have decreased growth capacity leading to entire absence of a given portion of the body, there "being no evidence that even its primordium was ever present." Streeter believes that these defects are involved in the constitution of the germ plasm. In discussing a case of anencephalus under his observation, he concludes that we deal with defective development dating back to the time of formation of the amniotic cavity and the laying down of the germ disk, and that such defect existed before the appearance of the notochord and for that reason certain parts of it were not involved. He feels that one must assume that but a small portion of the

anterior part of the germ disk was affected in such a case of anencephalus, comprising the cells that form the oral end of the medullary folds and sparing the primordia of the eyes.

Such a view of localized developmental defects would seem to apply in this case, as otherwise explanation of anencephalus in one of identical twins, the other being structurally normal is difficult to provide. It would seem that a disparity in the vitality of certain structures in one twin could occur locally, resulting in anencephaly, whereas the other twin might not be so affected, and would go on to normal development.

Acknowledgment is made to Dr. R. Gordon for permission to present this case.

REFERENCES

(1) *DeLee, J. B.:* Principles and Practice of Obstetrics, ed. 4, Philadelphia, 1925, W. B. Saunders Co. (2) *Döderlein, A.:* Handbuch der Geburtshilfe, Munich, 1915, J. F. Bergmann. (3) *Dietrich, S.:* Zentralbl. f. Gynäk. **38**: 587, 1914. (4) *Quigley, J. K.:* Am. J. Obst. & Gynec. **29**: 354, 1935. (5) *Streeter, G. L.:* Contrib. Embryol. **22**: 1, 1930.

185 North Wabash Avenue
104 South Michigan Avenue

CHORIONEPITHELIOMA FOLLOWING FULL-TERM PREGNANCY*

A Case Report

Clifford B. Lull, M.D., Philadelphia, Pa.

(From the Department of Obstetrics and Gynecology, Pennsylvania Hospital)

CHORIONEPITHELIOMA is associated in most minds with hydatidiform mole, and although the literature shows that a certain percentage does occur after full-term gestation, nevertheless, inquiry among various members of this society elicited the information that very few had seen chorionepithelioma following normal pregnancy. Inquiry also among the larger clinics in the country, has failed to reveal a very frequent incidence. It was therefore thought advisable to report this case to call the attention to the fact that bleeding following pregnancy should be looked upon with suspicion. A search of the records of the Philadelphia Lying-In Hospital shows no case of chorionepithelioma following a full-term pregnancy. All cases of chorionepithelioma recorded followed abortions or hydatidiform moles.

Mrs. M. D., aged twenty-nine, first consulted me when she was approximately three months pregnant. She was a nulliparous patient who had had influenza in 1918, tonsillectomy in 1926, and an appendectomy in 1928. There were no other serious illnesses or operations. Her periods had been established at the age of fourteen; had always been regular; normal in amount and duration. Her last period was Dec. 26, 1933, and her expected date of confinement, Oct. 2, 1934. This patient was seen with regularity during the rest of her pregnancy, and at no time had any disturbing symptoms more than the usual discomfort associated with pregnancy. Her blood pressure, urine, and other findings remained essentially normal.

She was admitted to the Lying-In Hospital private service on Oct. 5, 1934. Her pains began at 5 P.M. and at the time of admission, were approximately five-minute intervals, lasting from twenty to thirty seconds. Fetal heart sounds were heard in the right lower quadrant and were of good quality. The blood pressure was 110/50.

*Presented at a meeting of the Obstetrical Society of Philadelphia, May 2, 1935.

Labor progressed normally and at 9 P.M. she was given vi gr. nembutal and 1/150 gr. of scopolamine. The scopolamine was repeated at 1 A.M. Analgesia was good, and at 4:30 A.M., Oct. 6, 1934, the head was presenting at the vulva in R.O.A. position. Under light gas anesthesia, a median episiotomy was done and the head was lifted off the perineum. Duration of gas anesthesia was twenty minutes. The third stage was uneventful, the placenta being delivered sixteen minutes after the baby. The usual ernutin and infundin were given. The child was normal and was sent to the nursery in good condition. The patient's puerperal period was uneventful. At no time during her confinement to the hospital, which lasted eleven days, was there any elevation of temperature or pulse. The perineum healed immediately and the lochial discharge was normal on all occasions. Both mother and child were discharged in good condition on Oct. 17, 1934. The patient was told to report for follow-up examination in four weeks, and her postpuerperal care was outlined before discharge.

The subsequent convalescence was normal until Nov. 7, when the patient began to bleed rather freely. She was put to bed, oxytoxic drugs were administered together with sedatives, and in two or three days the bleeding stopped. No pelvic examination was made at that time. The patient again resumed her household duties which were limited to caring for the child and very minor household details.

On the thirteenth of November a sudden hemorrhage occurred, which was severe. She was immediately hospitalized, and at the time of admission she was in very slight shock. Intravenous injection of glucose together with stimulation was ordered, and the vagina packed temporarily. Six hours later, when the pulse and temperature were normal, she was taken to the operating room and under light gas anesthesia the vaginal packing was removed. The cavity of the uterus was explored with a blunt placental forceps and a few small shreds of decidual tissue removed. Examination under anesthesia showed involution of the uterus to be normal, and no adnexal masses. The uterus was packed, together with the vagina, and the patient returned to her room in good condition. The blood count the following day showed 64 per cent hemoglobin and 3,000,000 red cells. The packing was removed at the end of thirty-six hours. There was no further bleeding and on November 22, she was discharged in good condition.

While in the hospital her secondary anemia was actively treated. She remained in bed from the time of her discharge and was not seen until November 29, one week later. At that time her pulse was running between 90 and 100, and her temperature was normal. But during the entire week at home there had been a slight bright red bloody discharge. As this seemed to be rather unusual, she was again admitted to the hospital, and examined under nitrous oxide anesthesia (this patient was very difficult to examine without an anesthetic). During the course of the examination there was a spurt of bright red blood from the uterus, so that the uterus was again packed to control the bleeding. The examination revealed no pathology that was palpable in the pelvis and the uterus was well involuted. Chorionepithelioma was suspected and a Friedman test taken at this time was shown to be positive in dilutions of 1 to 20.

The quite typical elevation of temperature occurred the following day and immediate operation was postponed while the patient was given transfusions and other supportive treatment. There was no further hemorrhage when the packing was removed.

Five days later, in spite of an elevation of temperature and pulse, under light nitrous oxide and ether anesthesia, the abdomen was opened. The uterus was small and firm. Over the right horn there was a slight adhesion between the omentum and the peritoneal covering of the uterus. Upon lifting the omentum up, a small area about one-fourth inch in diameter was found with a bluish discoloration, and the peritoneal covering of the uterus almost perforated. Panhysterectomy was done as rapidly as possible and the patient left the operating room in good condition. Post-

operative convalescence until December 23, was more or less uneventful. The temperature receded and the pulse came down to about 90. The wound healed by primary union, and there was no unusual abdominal symptoms.

On December 30, sixteen days after operation, the temperature was normal and the pulse 96. On December 31 the patient began to cough and had definite pulmonary signs. X-ray of the chest on Jan. 3, 1935, by Dr. Paul Bishop, showed a great deal of mottled infiltration throughout both lungs, but more extensive on the right side and especially marked at the right base. His opinion was that this was a metastatic lesion. Reexamination on January 8 showed a distinct increase in amount of lung infiltration. Dr. Bishop's opinion was that the major portion of the pulmonary lesions was metastatic in origin. Patient's condition became gradually worse and by January 11, had definite signs of metastasis to the brain.

Death occurred on Jan. 13, 1935. Autopsy was not permitted.

Pathologic examination by Dr. John Bauer showed the uterus to be normal except in the region just anterior to the right horn where the surface was of a dark reddish blue color and the tissue definitely fatty. Here also there were two hemispherical nodules projecting above the surface of the organ. One of these nodules, the smaller, was 8 mm. in height and measured 12 mm. in diameter. The top was very soft and brown as though necrotic. There was also a firm pinkish nodule 4 mm. in height and diameter projecting from the upper surface of the right tube just proximal to its fimbriated end. The mucosa of the cervix and of the lower third of the uterus was normal in appearance. Microscopic examination showed a typical chorionepithelioma.

1731 PINE STREET

SPONTANEOUS EVOLUTION OF A TRANSVERSE PRESENTATION*

WILLIAM G. FRASER, M.D., BROOKLYN, N. Y.
(From the Department of Obstetrics, Norwegian Hospital)

TRANSVERSE presentations are of occasional occurrence, the statistics showing that in about one case in 200, the shoulder presents. Transverse presentations which correct themselves spontaneously are of exceedingly rare occurrence, this happening about once in 5,000 cases.

The case to be presented is of particular interest in that the baby weighed 3,262 gm., this weight being exceeded in the cases in the literature, by that of Busch 3,500 gm., and that of Herrgott 3,300 gm. Moreover, the entire mechanism was completed in forty minutes.

Mrs. D., forty-two years old, a white female, para viii, was admitted to the Norwegian Hospital at 2:00 A.M., Sept. 8, 1933, in labor. Her previous pregnancies, with the exception of the last, had all terminated spontaneously and each puerperium was afebrile. The one abnormality was a placenta previa lateralis, treated by rupture of the membranes and subsequent spontaneous delivery.

The patient's antecedent history was essentially negative and had no bearing on the case. Last menstrual period Nov. 17, 1932. Calculated term, Aug. 24, 1933.

She had had no prenatal care, but upon the onset of labor, at 9:00 P.M., called her local doctor who examined her vaginally, ruptured the membranes artificially, and then with obvious excitement, told her that something was wrong, and suggested hospital-

*Presented at a meeting of the Brooklyn Gynecological Society, April 5, 1935.

ization. An ambulance was called, and the examination by the ambulance surgeon at that time showed the patient in active labor, a transverse presentation, fetal heart sounds absent, and by rectal examination, the presence of a hand prolapsed through a cervix 4 to 5 cm. dilated.

Upon admission to the hospital, the routine physical examination revealed no gross abnormalities in the cardiovascular, respiratory, or nervous systems. Abdominal palpation showed strong abdominal musculature, absence of either fetal pole in the fundus, a head lying in the right iliac fossa, the breech lying in the left iliac fossa, and the fetal back directed anteriorly.

The pelvic measurements were normal.

A vaginal examination revealed a prolapsed left hand through the cervix, which by this time was almost fully dilated. A loop of the umbilical cord was also prolapsed. This was not pulsating.

A diagnosis of right acromio dorsal, anterior position, with prolapsed left hand and cord and dead baby was made. A podalic version was suggested.

However, the uterine contractions then increased both in intensity and frequency, and the patient in spite of being cautioned, began to bring her voluntary muscles into play. The result was that after a few contractions, the prolapsed left hand appeared at the vulva and with each succeeding contracton, more and more of the arm became visible, until the left shoulder slipped into view from beneath the symphysis. Then, still under the influence of the strong uterine contractions, the child began to rotate upon its vertical axis, the head moving from the right iliac fossa anteriorly until it came to rest overriding the symphysis pubis, and the breech moving posteriorly until it came to lie in the region of the promontory.

With the angle between the shoulder and the neck (which by this time had become considerably elongated) remaining the fixed point, the uterine contractions produced an extreme lateral flexion of the trunk, with the concavity directed toward the direction of the prolapsed arm. With descent into the pelvis being forced by the strong uterine contractions, there resulted, with a movement similar to extension in an occiput anterior presentation, first the left lateral aspect of the thorax followed by the left lateral aspect of the abdomen, and finally the left buttocks protruded from the vulva.

A second rotation now took place, the body rotating anteriorly through 90 degrees, so that both buttocks presented at the vulva.

The next contraction produced the delivery of the breech. An examination to determine the cause of delay following this revealed that the right arm had become extended over the head. This was swept down over the face, and with the use of the Mauriceau maneuver, aided by suprapubic pressure, the head was delivered.

There were no lacerations. The placenta separated spontaneously ten minutes later and was expressed by a modified Credé. The blood loss was 300 c.c.

The entire mechanism, from full dilatation to the delivery of the placenta, occupied only forty minutes. The baby was stillborn. It weighed 3,262 gm. There was nothing corresponding to a caput succedaneum on the shoulder that was prolapsed. The neck was elongated, and the head inclined toward the right shoulder. The upper part of the chest showed numerous ecchymoses. Autopsy of the baby was refused.

The puerperium was uneventful, and the patient was discharged on the tenth day after an uneventful uncomplicated convalescence.

4520 Fourth Avenue

BRENNER TUMOR OF THE OVARY*

PHILIP HAMBLIN SMITH, M.D., F.A.C.S., EVANSTON, ILL.
(From the Department of Obstetrics and Gynecology, Evanston Hospital)

THE patient, a widow, aged forty-five, was first seen in February, 1935, at which time she gave the following history: One pregnancy carried to term and delivered normally fourteen years ago. Menses began at thirteen and have been regular every twenty-eight days until three months ago when they began a week early and with a considerable increase in flow. The two subsequent periods were likewise excessive in amount. She has had no operations and denies disease other than measles and influenza.

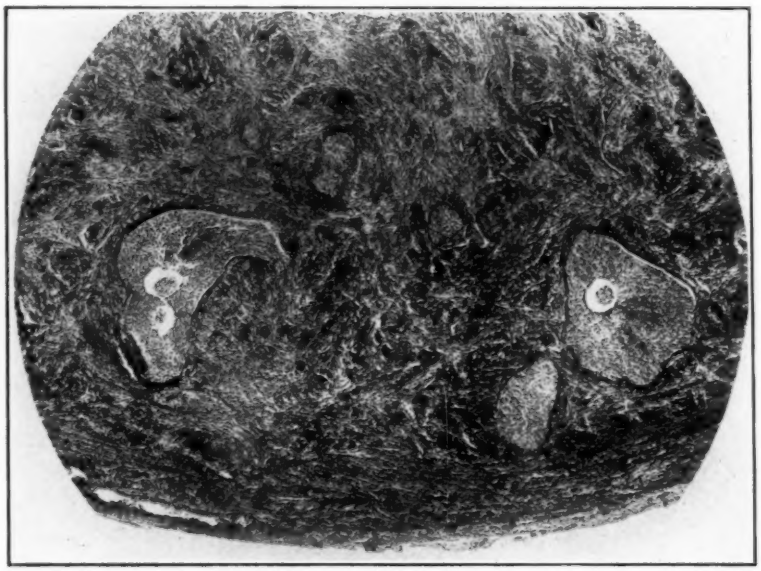

Fig. 1.—Showing coarse interlacing bundles of fibrous connective tissue and two nests of epithelial cell masses with their cystlike cavities containing "foam cells."

She presented herself at this time because of this increase in menstrual flow and what she described as a tight feeling in the pelvis.

Examination revealed a moderately relaxed vagina. The cervix was normal. The uterus was anteflexed, very irregular, mobile, and three or four times normal size. The right ovary seemed some larger than normal. The left adnexa were negative.

The Wassermann and Kahn tests were negative.

The urine was normal. The blood count showed 4.14 red blood cells, 8,500 white blood cells, and hemoglobin was 65 Sahli units.

Operation.—April 3, 1935. Median laparotomy. The uterus was found to be four times normal size and contained numerous subserous fibroids. The right ovary was three times normal size and contained a mass resembling a fibroma. Gallbladder and appendix were normal.

*Presented at a meeting of the Chicago Gynecological Society, May 17, 1935.

Subtotal hysterectomy with removal of the right adnexa was done.

The postoperative course was uneventful and the patient was discharged on the fourteenth postoperative day.

Pathologic Examination (Microscopic).—Sections of the ovarion tumor show a structure which is predominately fibrous but which contains numerous thick cords and nests of large, polyhedral, epithelial cells. These cells are pale with distinct cell outline and almost clear cytoplasm. Their nuclei are oval, pale, contain small, dark nucleolus and a few fine granules of chromatin and occupy about two-thirds of the cell. Few mitotic figures are seen and the cells are remarkably uniform in size and staining reaction. A few of these cell masses contain one or more minute, cyst-like cavities, incompletely filled (shrinkage) with lipoid-laden "foam cells" and granular detritus. These cavities are apparently formed by fatty degeneration of centrally located epithelial cells since evidence of such degeneration is seen in other cells bordering on the "cysts." No true alveolar structures are seen in any part.

The stroma which constitutes over nine-tenths of the tumor consists of coarse anastomosing and interlacing bundles of fibrous connective tissue. A section through the ampulla of the tube shows two small compact masses of epithelial cells, similar in every respect to those of the ovarian tumor, which are embedded just beneath the peritoneum on the anteligamentous surface.

Diagnosis.—Encapsulated "follicular oophoroma" (Brenner) of the ovary. Minute "oophoroma" nodules on the surface of the fallopian tube. Adenomyomatosis of the uterus. Premenstrual hyperplasia of fundic endometrium.

636 CHURCH STREET

King, Arthur G.: The Friedman Rabbit Ovulation Test in Differential Obstetric Diagnosis, J. Lab. & Clin. Med. **19**: 1033, 1934.

The author has collected 4,515 cases of Friedman tests from the literature to March, 1933, and has added 86 cases of his own. The gross error is 3.9 per cent. The false negative findings he divides into three classes: 82 due to limitations of the test, 13 to technical flaws, and 54 cannot be explained. The latter group with 26 false positive findings makes an error of 1.8 per cent. There were 48 cases in class three in the author's own series where early tests were negative while later tests were correctly positive. In 7 cases reported, the test was negative until the fourth to the sixth month. Therefore, a negative reading does not rule out early pregnancy.

In ectopic pregnancy a positive reading indicates that live chorionic tissue has been in existence within the last seventy-two hours; a negative test means little. Of 57 ectopics reported only 41 gave positive reactions and the author adds 2 in his own series. In hydatid mole and chorionepithelioma, perfect satisfaction is given in all reports. Carcinoma of the uterus occasionally gives a positive Aschheim-Zondek test although usually a negative Friedman test. One case in the series was negative and another positive (acanthoma). In obese patients, for the differential diagnosis between fibroids, ovarian cyst, and pregnancy, the test was very helpful. There were 13 such cases all correctly positive or negative, as proved subsequently. The author concludes that the test is a valuable aid in diagnosis provided its limitations are recognized. A positive test indicates usually, but not always, the presence of live chorionic tissue. It may not become positive until pregnancy is well advanced, and if positive may not necessarily mean that the fetus is alive. The test should assist but not supplant the usual diagnostic technic.

W. B. SERBIN.

Society Transactions

AMERICAN GYNECOLOGICAL SOCIETY

SIXTIETH ANNUAL MEETING

Hot Springs, Va., May 27, 28, 29, 1935

The following papers were read and are published in the Journal, except as noted. Abstracts of the discussions are presented and the complete proceedings will appear in the current volume of the Society's Transactions. The President, Dr. Brooke M. Anspach, of Philadelphia, Pa., was in the chair.

1. **Further Studies on the Mechanism of Labor by Means of the Roentgen Ray.** Drs. William E. Caldwell, H. C. Moloy, and D. Anthony D'Esopo, New York City. (For original article, see December issue.)

2. **Clinical and Bacteriologic Observations in Trichomonas Vaginitis.** Drs. Edward Allen, Lloyd B. Jensen, and I. H. Wood, Chicago, Ill. (By invitation.) (For original article, see page 565, October issue.)

DISCUSSION

DR. CARL HENRY DAVIS, MILWAUKEE, WIS.—The typical vaginitis may be the result of a symbiosis since we consistently find both trichomonas and some type of streptococcus.

If we follow up the obstinate cases, as Dr. Allen has done, we are going to find that a high percentage of these constantly recurring cases must be ascribed to the male prostate as a possible source of reinfection.

Unless we get at the original source we will not clear up the infection in some patients regardless of the type of local treatment. I believe that local treatment should be kept up almost daily for the first week or two, and then be tapered off gradually. Some type of home treatment is necessary. There are a number of new preparations which have some advantages over the earlier forms of treatment.

DR. NORMAN F. MILLER, ANN ARBOR, MICH.—Our experience with this type of vaginitis coincides with that of Dr. Allen. Most of the patients respond to some form of local therapy. We have not, however, noticed any severe urinary symptoms except in the presence of an active vaginitis. Neither have we noticed any disturbance in menstruation which we felt could be attributed to trichomonas infestation.

The specificity of the flagellates in trichomonas vaginitis has often been questioned. The possibility of symbiosis has been mentioned frequently. Bacterial association to the extent of true symbiosis is not uncommon. It is known for example that anerobic microorganisms are able to live in the presence of air if they are permitted to grow in association with aerobic microorganisms (tetanus bacilli when grown with diphtheria bacilli). Whether the disease under consideration is an example of a true symbiosis between flagellates and streptococci remains to be seen. While this work strongly suggests such relationship, caution is necessary for nonsymbiotic

association of organisms is common. Furthermore, the normal vagina may harbor streptococci of various strains including the viridans.

The presence of trichomonas in the male urinary tract occasionally has been noted. One patient seen in the genitourinary service in our own hospital had a severe pyelitis apparently due to trichomonas. Unfortunately no cultures were made, but in the light of the work just reported, it is possible that streptococci were present as the fundamental cause of the kidney infection. Isolation from the male urinary tract of streptococci similar to those associated with the flagellates in trichomonas vaginitis strongly adds to the evidence of a true symbiosis.

The occurrence of cellulitis in several of these patients is extremely interesting. It seems logical that this should be due to the associated streptococci, but I wonder why it does not happen more frequently. Many of my most severe cases have been in pregnant women. If further study convinces Dr. Allen and his colleagues that the *Streptococcus viridans* is a necessary factor in trichomonas vaginitis, the potential seriousness of this condition as a complication of pregnancy is at once apparent.

DR. JOSEPH B. DeLEE, CHICAGO, ILL.—I would like to emphasize the necessity of building up the general system of the patient in trying to cure trichomonas. I cured three patients permanently by giving thyroid. The basal metabolism was found to be very low and within three weeks there was a marked change. That was five years ago, and they have remained cured.

The study of the husband in these cases is important when one considers the intimate relations present.

DR. GEORGE GELLHORN, ST. LOUIS, MO.—It seems to me that clinical observations do not bear out the assumption that it is a streptococcus rather than the trichomonas which causes the condition under discussion. That assumption which has been made repeatedly in the past was based upon a statement accredited to Donné, of France, the discoverer of the trichomonas. In his original communication published in 1836, it will be noted that he did not find these trichomonads in the normal vagina as harmless parasites but only in purulent discharge. It would therefore appear that the trichomonas is the primary cause of the irritation, and that this irritation activates the ubiquitous streptococcus in the vagina and then gives rise to the complications mentioned by the speaker.

Another proof that this vaginitis is due to trichomonas is the result of treatment. The therapy initiated by Hoehne, of Germany, some twenty years ago has, with minor changes, been used until recently. It consisted in washing, and sometimes even scrubbing, the vagina with soap and water and then flooding it with a bichloride solution. This old method is extremely unreliable and in many instances has to be continued for months. The reason for this is clear. Were the streptococcus the causative agent, one or a few bichloride applications would kill or weaken the bacteria. The trichomonads, on the other hand, are not affected. Only when I introduced an entirely new principle into the therapy by insufflating an amebacidal specific into the vagina, an arsenical which affected only the trichomonads but not cocci, were the results changed. In very favorable cases the discharge would disappear overnight, and in the large majority of instances only three or four treatments were required to produce cure.

The prevention of trichomonas vaginitis is also pertinent to the subject. It has been claimed that these amebas came from the rectum, although there were some questions raised because the rectal and vaginal trichomonads were supposed to differ in the number of flagella. I am not competent to say whether this distinction is true nor am I prepared to say whether prophylactic oral administration or rectal enemas containing stovarsol have any protective value; but in at least one case of frequent

recurrences I could determine definitely that each return of the trichomonas vaginitis followed an intestinal upset and attack of diarrhea.

DR. FRED L. ADAIR, CHICAGO, ILL.—The few remarks I have to make are based on the work of Dr. Hesseltine at the Chicago Lying-In Hospital, who has been interested in infections of the lower genital tract for some time past. There are several etiologic factors which appear to be of great importance. First, it must be recognized, I think, that the trichomonas are not found in association with normal vaginal flora, that there are other associated bacteria. These associations are practically constant and this is emphasized by the fact that so far it has been apparently impossible to culture the trichomonas isolated from other bacterial forms. Perhaps this is explained by the supposition that other forms of bacteria are needed, so that apparently bacteria other than the normal bacteria of the vagina are necessary for the development of the trichomonas. Furthermore, the hydrogen ion concentration is altered in this type of infection. The histology also becomes important; apparently from the more or less mechanical alteration and the breaking down of the normal epithelium, with alteration in the cells themselves, the invasion of infective agents is rendered possible. By removing small pieces of vaginal tissue with a punch we find that there is a loss of epithelium. We find definite inflammatory reactions in the subepithelial or submucous layers. In association with this we have not been able to demonstrate the trichomonas in the tissue but have been able to demonstrate bacteria, indicating that the bacteria themselves are invasive rather than the trichomonas. Third, by the alteration in the tissue chemistry itself, apparently in the lowering of the glycogen.

Treatment has been based upon the supposition that one could destroy these organisms by antiseptics, also by the use of coagulants, which would tend to increase the surface resistance; also by changes in the hydrogen ion concentration of the vaginal secretion; also by filtrates and other means of increasing general or specific immunity.

In the treatment we have tried innumerable things. Control methods were used, and it was found that apparently sodium bicarbonate by altering the pH of vaginal secretion seemed to work equally well as the stovarsol, so it was concluded that the latter was not necessary.

Stimulation of the growth of the normal vaginal bacillus is important in checking these infections, and this can be done by increasing the carbohydrate content of any agent which is applied to the vagina. Inasmuch as these infections are common and no form of yeast ferments lactose, it has been selected as an agent which favors the growth of the vaginal bacillus which tends to increase the sugar content of the vaginal epithelium and also tends to restore a normal pH in the vagina. By combining citric acid with lactose 5 per cent and 95 per cent respectively, favorable results have been obtained.

DR. JAMES R. GOODALL, MONTREAL, CANADA.—There can be little doubt that behind every case of trichomonas vaginitis, there is an individual susceptibility, as in all other infections.

In many instances of this disease, local treatment, however prolonged, may not produce a cure, until some elevation of the general tone of the body is brought about by appropriate remedies. In one instance, large doses of iron, in others, sun treatment, proved efficient when combined with topical care.

In my experience, there have been recurrences due to prostatic trichomoniasis in the husband. But that this is not a common source of infection is proved by the frequency of the disease in young virgins. That contact is a fruitful cause of spread is shown by the incidence of the same disease in two or three members of the same family, chiefly children.

I have studied the variations and find certain morphologic differences as shown in Fig. 1. *A*, shows the type of trichomonad usually found in the ordinary case of vaginitis. *B*, shows the rarer type, which I have called the "windmill"; the flagellae which are grouped at one end spin very rapidly. The "angler," is a much rarer form, found only twice in over 300 cases. The organism operates this flagellum rhythmically, and as perfectly as an angler casts his "fly." The movement is never fast, but almost deliberate. It slows perceptibly on cooling. The end of the flagellum is armed with a nob. Whether this is a sucker or not, cannot be detected. The "spin-wheel," having all its flagellae beating in one direction, spins about rapidly thereby causing currents to approximate food. The "seal" is the most interesting of them all. Its larger base is more or less fixed to the substance on which it rests, but its upper half is as mobile as the head of a seal, and closely resembles the latter in all its movements. Whether these forms are conditioned by soil and food is at present impossible to determine. But whatever the cause, mixed types are not found in the same clinical case. Though the organisms may vary much in size in the same case, they are true to type. This rather leads one to believe that at least the types described are generic rather than developmental. The

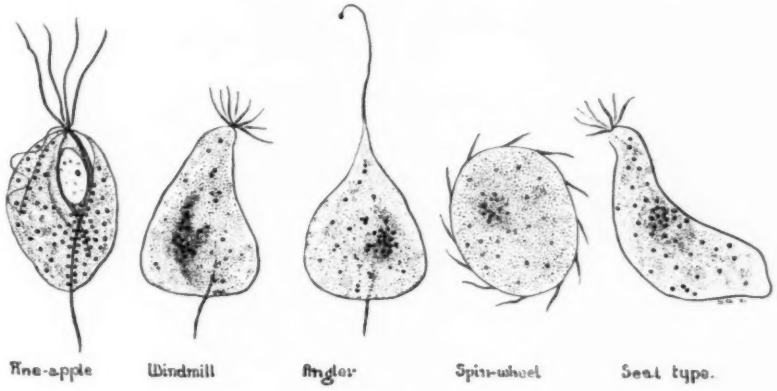

Fig. 1.

corporeal properties of the different types of trichomonad seem fairly uniform, but the differences are chiefly in the distribution of the flagella, whose functions seem to be both auto- and circumferential locomotion for procuring sustenance.

DR. ALLEN (closing).—I am very much interested in the discussion of the types of trichomonas that Dr. Goodall has shown. I wonder if these various forms of trichomonas are not similar to the change in form of the streptococci? When these organisms are cultured they assume a great many diverse forms and I wonder if this change in type or structure of the trichomonas may not be due to changes in the habitat?

The report of Dr. Adair that there were organisms in the subvaginal tissue is very interesting, especially in association with the bladder symptoms. Recently we have been cystoscoping these patients and quite a number of these women, even without urinary symptoms, have a condition that resembles inflammation in the trigone. We have also noticed in several, little petechial hemorrhages scattered over the fluffy, edematous bladder mucosa.

Replying to Dr. Gellhorn, I did not mean to say that these organisms are the cause of the condition. I just wanted to report their association with trichomonas.

4. **The Treatment of Dysmenorrhea by Presacral Sympathectomy.** Dr. Floyd E. Keene, Philadelphia, Pa. (For original article, see page 534, October issue.)

DISCUSSION

DR. OTTO H. SCHWARZ, ST. LOUIS, MO.—I believe it important to call attention to one phase of dysmenorrhea which should be considered before such an operation as presacral sympathectomy is performed.

It is known that essential dysmenorrhea in a considerable percentage of cases is due to allergy. In 1931, D. R. Smith, my associate, reported 12 cases: 8 of the patients were cured completely by withdrawal of the food to which these patients were sensitive. There were 4 partial cures. Since that time Smith has had 10 more patients who are entirely free of symptoms since the allergic factor has been withdrawn. In 5 other cases there was definite improvement, and there were also 5 failures. With these figures in mind, I think it is very important to rule out allergy before any radical operative procedure is carried out.

DR. CHARLES A. BEHNEY, PHILADELPHIA, PA.—About four years ago I began to perform this operation for patients with intense pain from carcinoma of the cervix. About three years ago we started to do some sympathectomies for dysmenorrhea and since that time have operated upon eleven patients, with four failures in securing complete relief. Sometimes we learn more from our failures than from our successes, and I feel that in these instances complete relief would not have been expected had they been thoroughly studied from urologic and orthopedic standpoints. This operation is indicated only in the type of dysmenorrhea that has been studied from every standpoint and cannot be cured by more conservative measures. There are patients who have pelvic pain due to lesions of the pelvic sympathetic nerves and who can be relieved only by excision of these structures.

The longest permanent relief which we have secured has been for three years.

DR. EMIL NOVAK, BALTIMORE, MD.—While I have performed this operation in only a few cases, it impresses me as a valuable addition to our armamentarium in the treatment of cases of very severe primary dysmenorrhea in which other measures have been unsuccessful.

The psychic factor is such an ever present one in the evaluation of treatment in cases of dysmenorrhea that one cannot set it aside in appraising the results of presacral sympathectomy. However, when one stops to think that this procedure is apparently capable of relieving the very genuine and very severe pain of advanced malignancy, there would seem little justification for skepticism as to its possibilities in dysmenorrhea. One would think that the operation would be hailed with delight, offering as it does a logical and yet not too radical means of treating the occasional severe and intractable case where constitutional, psychotherapeutic and other measures have been without avail.

Technically the operation may be looked upon as a rather simple procedure, and when properly done, apparently producing no harmful effects. Where unusually severe dysmenorrhea is the chief symptom of otherwise unimportant pelvic abnormalities, such as displacements, so that there is some doubt as to whether correction of the latter will relieve the severe pain, presacral sympathectomy may well be combined with other operative measures, such as suspension, which may be indicated.

5. **A Study of a New and Potent Ergot Derivative.** Drs. Fred L. Adair, M. Edward Davis, M. S. Kharasch, and Romeo R. Legault, Chicago, Ill. (For original article, see page 466, October issue.)

DISCUSSION

DR. M. PIERCE RUCKER, RICHMOND, VA.—In 1921, Dr. Haskell and I became very much interested in the action of pituitrin, and one method of approach was to compare it with the action of ergot. We tried three different preparations, the fluid extracts and two so-called purified preparations. We tried them on isolated strips of uteri and also upon uteri intact in dogs and cats, and in two instances I tried it antepartum with a bag in the uterus, also in a number of cases after the third stage of labor using the external method of Rübsamen. Our results so far as ergot was concerned were extremely disappointing. In the first place we could not standardize preparations of ergot, and it was necessary to use, in order to get any effect on the animal's uterus, as much as twenty times the amount of ergot as of pituitrin, and in some cases as much as thirty-two times the amount of pituitrin. The effect on the human being was even more variable. In the antepartum cases I could get no appreciable effect, although there were only two. In some cases immediately postpartum we could get some demonstrable results with as much as one or two drams of fluid extract of ergot, but it was not as successful as pituitrin.

With regard to the method used by Dr. Adair, Koff several years ago stated that he thought that the immediate use of a bag postpartum was a dangerous thing; in a previous communication I think Dr. Adair used the bag immediately after the third stage of labor. In the present paper I believe he has recommended it after the fifth or sixth day. I am wondering if he found any bad effects from this method when used immediately after delivery?

This work is most important both as to the method used and because Dr. Adair has given us a very reliable and constant ergot preparation. I have not yet been able to test it out with laboratory methods but clinically it seems to work very well indeed. I have used it immediately after delivery of the placenta. The uterus becomes extremely firm and stays so for several hours after delivery. It gets rid apparently of that secondary oozing that one often finds after putting the patient to bed after having given her a dose of pituitrin.

DR. ADAIR (closing).—Naturally there are many things in the paper which I did not have time to present today. We have used this method during labor, and we do use it immediately after the first stage, but for the most part our studies have been on the sixth to the eighth day postpartum uterus, and I might say that our cases have been selected with extreme care. We have used only multiparous women where there has been no morbidity. In over 200 cases there were no complications which one might apprehend. We did not inject this without some apprehension and have maintained, as I say, a very careful selection of the cases, with scrupulous technic.

Our conclusions are that we have isolated in crystalline form the active principle of ergot which is responsible for most, if not all, of the desirable oxytocic effect of ergot. We have designated this substance as ergotocin. It is potent in minimal doses by various methods of administration. It does not deteriorate readily and is constant in its action. It is relatively free from untoward or undesirable effects. Its margin of safety is very great as the degree of toxicity is very low. It has no apparent detrimental effects upon respiration, pulse, blood pressure, or urinary output. This emphasizes the value of its use in cases having evidence of cardiovascular-renal diseases or toxemias where oxytocic action is required. We are not advocating its use during the third stage of labor, but believe it may be used during this stage as safely and more effectively than any other known oxytocic drug. It is extremely valuable in stimulating uterine contraction in the immediate and remote postabortal and postpartum periods. Its prompt effect in producing tetany and contraction of the uterus, and its prolonged action, make it of special value in the management of postpartum hemorrhage. With the isolation of ergotocin, the age-

old problem concerning the oxytocic principle in ergot apparently has been brought to a close. We now have the desirable, potent, oxytocic activity in ergot isolated in a crystalline material, stable and nontoxic. Ergotocin can be used safely whenever an oxytocic therapy is indicated.

6. **Hypothyroidism as a Problem in Women.** Dr. Carl Henry Davis, Milwaukee, Wis. (For original article, see page 570, October issue.)

DISCUSSION

DR. L. A. CALKINS, KANSAS CITY, MO.—From our very limited experience of 126 cases it would seem that thyroid dysfunction is less frequent in Kansas City than in Milwaukee. Dr. Davis has very properly pointed out the necessity for the greatest of care in making the test as the results are materially affected by congestion of the breasts, mild uterine contractions, and other very minor disturbances. It is, therefore, not safe to depend upon the results as reported by the average laboratory technician.

In 126 cases we found 10 per cent above the normal range, 63 per cent within the normal range, and 26 per cent below the normal range. This latter group were all postpartum cases. None of the 126 received any treatment.

From this very limited experience we have two impressions with respect to the problem in the Kansas City area: First, that mild degrees of thyroid dysfunction may be contributory to certain of the variations commonly noted in labor and the puerperium; second, that the problem of thyroid dysfunction in the puerperal state is deserving of further investigation.

DR. J. C. LITZENBERG, MINNEAPOLIS, MINN.—I have been attracted to this disturbance in women from three standpoints: first, the standpoint of sterility and habitual abortions; second, the standpoint of various disturbances of menstruation; and third, the "general run down condition," as the patient usually calls it.

In 1926, I wrote on the subject of the relation of sterility to hypothyroidism and found in some seventy cases that 50 per cent of all sterile women had a low basal metabolism and by treatment with thyroid extract one-third of those women became pregnant. It should be remembered that we are in the goiter area the same as Milwaukee, and whether these things apply in the nongoiter areas I do not know. Of the unmarried women with low basal metabolic rate 40 per cent had disturbed menstruation.

In 1929, Dr. Carey cooperated with me in studying these cases from a medical standpoint, and we found in that series that 57 per cent of all women seeking help from sterility had a low basal metabolic rate and 37 per cent became pregnant after treatment with thyroid. Forty per cent in the first group had disturbed menstruation, and in this group 36 had a low basal metabolic rate; and 45 per cent as compared to 50 per cent in the previous group were sterile. Dr. Carey studied this subject from the standpoint of the internist entirely and in some 700 cases of women seeking advice for various disturbances found that 56 per cent of married women with a low basal metabolic rate were sterile. The average sterility rate is 13 per cent among American women. This work was summarized last year by Carey and Bromfield, both of the Nicollet Clinic. After summarizing the three previous papers of Litzenberg and Carey and adding the subsequent cases they found that 52.8 per cent of all the women had a low basal metabolic rate, and 39.7 per cent had menstrual disturbances.

The result of thyroid treatment of these conditions in the whole four series was that 34.3 per cent of the sterile women who had low basal metabolic rates,

became pregnant; and of all other symptoms for which they came, nervous disturbances, menstrual function, etc., 62.8 per cent were improved by treatment.

I have been particularly impressed by the fact that women on thyroid treatment even if they did not conceive were very much improved in their general health. We have had equally good results in women having habitual abortions; approximately 70 per cent with a low basal metabolic rate have been carried through subsequent pregnancies successfully. I agree with Dr. Davis that certainly in the goiter areas, basal metabolism rates should be taken frequently upon many gynecologic and obstetric patients. I do not do it routinely, but where there are certain indications it is done and in most of the cases of habitual abortion the patients carry through to full term. In 62 per cent of the women with menstrual disturbances they are improved or cured.

DR. PHILIP F. WILLIAMS, PHILADELPHIA, PA.—The explanation which Dr. Davis has given for the increase in the number of women with hypothyroidism in the Milwaukee area is intriguing. Presumably continued studies of the women in that district who have been subjected to iodine therapy during adolescence will confirm his explanation. The Atlantic seaboard did not suffer the destructive geologic influences of the Permian Age as did the Midwest, and consequently we do not have the same problem in and about Philadelphia as they seem to have in Milwaukee and adjacent areas. It is not surprising, therefore, that a cursory survey of the metabolic readings in two Philadelphia hospitals shows that less than 10 per cent have basal metabolic readings of lower than minus 15. Hypothyroidism is not a very frequent problem in obstetrics or gynecologic practice in Philadelphia, nor is hyperthyroidism, although we do have some instances in migrants. It is found sometimes in nervous, mental, cardiac, and anemic conditions and also in subnormal constitutional states. In Philadelphia we see low basal metabolic readings in sterile women and in some parous women with stillbirths. In some of these instances there may have been a deficient germ plasma in the hypothyroid woman. We have sometimes found that thyroid therapy stimulated the basal metabolic rate to a certain degree but did not bring it back to normal. In some of those cases pituitary preparations have been of assistance. Just what reference Collip's work bears to this problem is speculative.

So far as having a definite reading in basal metabolic studies, and as to what constitutes hypothyroidism, we believe that a woman with a minus 2 or 5 who is sluggish and easily fatigued is to be considered a hypothyroid case just as is a woman with a low basal metabolic rate, and they are often much benefited by thyroid therapy.

Three times I have seen craniorachischisis occur in fetuses of women with a low basal metabolic reading; in two of these cases the women conceived again and delivered normal children without any thyroid therapy.

DR. GRANDISON D. ROYSTON, ST. LOUIS, MO.—Most internists attach little importance to basal metabolic readings of less than 20 per cent, yet I agree with Dr. Davis that there is a fairly large group of women, whose readings are not so low, who improve under thyroid medication. For some years I have been doing routine basal metabolism readings on all obstetric patients and on those gynecologic patients whose symptoms or physical findings suggested thyroid dysfunction.

Our findings agree fairly closely with those of Dr. Davis.

A group of 231 gynecologic patients studied by us, selected because of the suspicion of thyroid dysfunction, showed minus readings present in 74 per cent of this number. Because of their being in a selected group, this figure is not a fair index as to the frequency of low basal metabolic readings.

The basal metabolic readings in the last 419 consecutive obstetric patients showed 63.4 per cent were on the minus side; 23.8 per cent were minus 10 per cent or lower. Weight played but little part in the basal metabolic rate, since in only the group weighing from 150 to 159 pounds did the plus readings exceed the number of minus readings. I might add that height played no part in the basal metabolic readings.

We have attempted to classify these patients according to types: the asthenic type showing genital deficiencies as congenital displacements, retrocession, elongated cervix, infantile uterus, contracted pelvis (chiefly of outlet), etc., plus evidences of congenital tissue deficiency in other parts of the body, as the narrow high hard palate, narrow costal arch, diastasis, splanchnoptosis, etc. Where evidences of congenital tissue deficiency of parts of the body not including the genitalia were present, the individual was classed as hyposthenic. Sthenic types showed none of these deficiencies, and hypersthenic showed some exaggeration of the normally physically well-developed person.

Among the 231 gynecologic patients, 18 per cent were classed as asthenic; 48 per cent as hyposthenic; 31 per cent as sthenic and 2 per cent as hypersthenic.

The 419 consecutive obstetric patients comprised 9 per cent asthenic; 48 per cent hyposthenic; 37 per cent sthenic; and 6 per cent hypersthenic, suggesting that asthenic types are possibly less apt to conceive.

Fatigue was present in approximately 50 per cent of our patients while 20 per cent complained of mental depression. Less than 2 per cent of the patients in our series complained of somnolence, whereas 40 per cent suffered from insomnia.

We attach much importance to the basal pulse, which is counted at the time the basal metabolic reading is determined, and we feel that this basal pulse is second in reliability only to the basal metabolic rate itself. The patient is taught to count her basal pulse in the carotid artery on awakening, twice weekly, and we have found it a valuable aid in helping to regulate her thyroid dosage.

Those patients Dr. Davis mentioned as having low basal metabolic readings and a fast pulse, did not do well under thyroid in our series, possibly because we did not continue its administration long enough. However, we feel that these patients should have malnutrition excluded as a possible factor. Such patients did better with iodine and a high fat diet under our care.

Dr. Litzenberg has emphasized the importance of hypothyroidism in connection with sterility. In this series there were 70 sterile patients. Of this number, the male factor was present in 13; in 5 others we were unable to complete the examination. However, of the 52 remaining patients, 53.8 per cent conceived and the largest group of conceptions was treated solely with thyroid and a high vitamin E diet. Of the sterility patients who conceived, more than 82 per cent received thyroid medication.

DR. JAMES E. KING, BUFFALO, N. Y.—I feel from my own experience that too great stress has been laid upon the value of the basal metabolic rate. At first I was inclined to have all of my cases tested by this method and I found, much to my surprise, that even in cases where the basal metabolic rate was not disturbed, the use of thyroid benefited my patient. At present I am not using the basal metabolic reading but feel that we can by questioning our patients get enough evidence to indicate a thyroid deficiency.

I give larger doses of thyroid than Dr. Davis gives, usually a grain morning and night, and then as the symptoms improve or a change is noted upon examination, the dose is decreased or increased as needed.

DR. EMIL NOVAK, BALTIMORE, MD.—Attention may again be called to the very obvious fact that in thyroid studies in cases of sterility the male partner is entitled to the same consideration as the female. In a couple which I recently

examined, the wife showed a metabolic rate of minus 45, but that of the husband was minus 55.

I agree with the previous speakers as to the frequent value of thyroid medication, although we know little as to the nature of the thyrogonadal relationship. While, in my experience, hypothyroidism is more often manifested by excess rather than deficiency or absence of menstruation, there are so many exceptions to this rule as to confuse our ideas concerning the mechanism which may be involved. The same is true as regards hyperthyroidism, which most frequently is associated with menstrual deficiency rather than excess. Perhaps the thyroid rôle is only an intermediary one, the real disturbance involving the thyreotropic hormone produced by the anterior lobe.

Certainly in Baltimore and vicinity we do not find anything like as high an incidence of hypothyroidism with sterility as Dr. Litzenberg finds in Minnesota. As a rule the gynecologist is rather grateful if he finds a very low basal rate in the sterile woman, for a logical course of treatment is at once indicated, with frequent success. Even with a normal rate, however, the judicious use of thyroid is fully justified, not only in sterility, but often in cases of habitual abortion. Just how it acts in the latter group no one knows, though there is some reason to think that its effect is upon the germ plasm. Embryologists now accept the doctrine of defective germ plasm as a cause of "idiopathic" abortion.

There are some women who menstruate but do not produce ova, thus accounting for certain cases of sterility. There are others who ovulate, but in whom the ova are of poor quality, unable to combine with spermatozoa. These, likewise, are sterile. In others the egg becomes fertilized, but the germ plasm is so deficient in quality that the pregnancy "peters out" prematurely, and this may occur repeatedly, as in habitual abortion. In still others the pregnancy goes to term, but the child is born dead or dies soon after birth. Finally, in the ideal cell union, the *vis a tergo* is sufficient to carry the egg throughout the normal human span. It is perhaps an effect upon this elusive factor of germ plasm which thyroid therapy brings about, so that there is full justification for the inevitable "pinch of thyroid" commonly added to other efforts at organotherapy.

DR. FRED L. ADAIR, CHICAGO, ILL.—In habitual abortion I had a number of cases that responded to the administration of corpus luteum and I think it is possible that the administration of thyroid extract might operate on the corpus luteum and accomplish this result in a different way.

I should like to refer to the administration of iodine to the mother and its effect upon the fetus. A number of years ago Dr. George Hudson carried out some rather extensive experiments upon rabbits. Of course, if iodine does not pass through the placenta we would not expect it to affect the fetus. He was able to demonstrate that inorganic iodine did pass through the placenta and consequently we felt that the chances were that in the human being it also might pass through the placenta. Its influence was demonstrated by the presence in increased amounts in the fetuses of animals who received it as compared with animals that did not receive it. It was also demonstrated by histologic examination showing a difference in thyroid of those who received iodine and those who did not.

DR. ROBERT T. FRANK, NEW YORK, N. Y.—This does not seem to me a problem that can be settled by statistical methods. Sometimes we can get more information by a few cases rather than by statistics.

On the Atlantic seaboard a 10 per cent minus or plus basal metabolic reading ordinarily has little significance. If it is minus 10 it is more apt to be significant as the newness of the examination has a tendency to increase the rate and therefore

signifies more than a plus reading. I feel that repeated tests are necessary before we consider it a disturbance of metabolism.

I agree fully with Dr. Williams that these minus grades can usually be favorably affected by increasing the caloric intake, the protein rather than the fat diet.

Another startling thing, as Dr. Novak has already mentioned, is that you see both amenorrhea and particularly puberty bleeding in patients who have the same clinical manifestations, namely lowered basal metabolism. I am not speaking now of these minor deviations, but of a minus 20 or 30.

The response to thyroid therapy is gratifying. That leads you to conclude that probably the thyroid is simply an index of a deeper lying disturbance, otherwise it should not manifest itself in these two diametrically opposite fashions. Therefore, at the moment we are probably merely at the threshold of recognizing the single something which however is based upon a more fundamental underlying trouble and probably the prepituitary.

I do not believe that doses of thyroid of one-fifth of a grain can really have an influence upon a lowered basal metabolism. A reading of minus 10, 20, or 30 requires ascending doses. Furthermore, it should be kept well in mind that thyroid medication lasts only a short time. If the patient is given thyroid for four or five weeks consecutively and you stop for ten days, the thyroid effect is over and is not carried beyond that definite influence. So while the basal metabolic test—and I think it is far superior to any other method of recognizing thyroid overaction or underaction—is extremely important, it does not afford conclusive evidence as to the location of the underlying condition.

DR. DAVIS (closing).—I believe that we are all in rather complete accord regarding the use of thyroid. Reference has been made twice in the discussion to one-fifth of a grain. Apparently there is a misunderstanding. I mentioned the fact that if a patient had a reading of minus 10 and had symptoms which suggested that there might be some thyroid disturbance, I start out by giving one-fifth of a grain U.S.P. per day and in two or three weeks repeat the basal metabolism test. Some patients have been relieved of symptoms and continue to have normal readings thereafter. Others have been found on repeat tests to be in the minus 20 group or lower. The largest dose I am giving at the present time is 5½ gr. per day of the Burroughs-Wellcome thyroid.

Dr. King and I have reversed our ideas. For years I believed that it was possible for me from a clinical point of view to determine which patients should have a metabolism test. In the last year and a half I have had basal metabolism rate tests done on 600 consecutive patients and the results have convinced me that it is not possible by any method other than the basal metabolic reading to determine safely which patients may be benefited with the use of thyroid medication.

The purpose of this paper was not to show that the metabolism rate is low in the vicinity of Milwaukee, but to emphasize again the fact that the men doing obstetrics in this country are the ones who may keep our population from developing thyroid disease such as they have in Switzerland, Bavaria, and other places where the people have been living for a thousand years or longer in goiter areas. With the information available at the present time I believe it is possible to keep from ever having a serious goiter problem in this country.

MR. VICTOR BONNEY, of London, spoke on the **Extended Scope of Myomectomy.**

Too many hysterectomies for fibroids are being done at the present time. That the ideal of surgery should be cure without deformity or loss of function is a truism, but apart from this the value of the uterus from the psychologic point of view needs

careful consideration. Women vary in their reactions to hysterectomy, but there is a very definite proportion who take the loss of the womb very much to heart; either because they are aware that to many men the idea of a woman not being "whole" is unattractive, or on account of the irrevocable sterility.

Myomectomy in the past has had a definitely limited scope, being restricted to cases where the tumors were single, or if multiple then superficially placed. Resenting this restriction I have extended the operation until now I am able to perform it on any case of fibroids if in my opinion conservation of the uterus is desirable. Myomectomy thus extended in scope should be in the repertory of every surgeon practicing gynecology, thus enabling him to do the best for any particular patient instead of being compelled to do a mutilating operation against his inclination, as is still far too commonly the case.

In a general way my rule is that in patients under forty-one years of age the preferential operation is myomectomy, while in patients over that age hysterectomy should be chosen. There are, however, exceptions to the rule; on the one hand, the relatively young woman who having had sufficient children wants to have her womb removed, and on the other the elderly woman who for private reasons, sentimental or otherwise, desires its conservation.

I have performed myomectomy 487 times. The fibroids were solitary in 237 cases, and multiple in 250 cases. Of the multiple cases the largest number of tumors I have removed from a single uterus is 125, and after that 92, 90, 80, 56, 55, 52, and 50, and so on downward.

I have had 7 operative deaths, a mortality rate of 1.2 per cent. No deaths have occurred in my last 200 cases, owing to improved technic.

In a Hunterian Lecture given at the Royal College of Surgeons of England in 1932 I showed that new fibroids formed in 5 per cent of the cases, but only in 3 per cent to the extent of requiring further operation. All these cases were patients who had developed fibroids at an exceptionally early age and to whom, therefore, a special fibroid-forming tendency must be ascribed.

Of 77 women within the childbearing age who wished and were in a position to have children 30 (or 39 per cent) did conceive. Seventy-five per cent of the deliveries were normal and 25 per cent were by cesarean section. The high percentage of cesarean sections was due to the relatively advanced age of the mothers and the specially great obligation to deliver a living child.

In regard to the technic I employ, I lay first emphasis on the myomectomy clamp invented by me. This instrument controls both uterine arteries at once, and in addition stops the entire blood flow from coming up through the cervix. The result is that when in addition the ovariopelvic ligaments are compressed by ring forceps the circulation through the uterus is completely stopped and the operation becomes bloodless. The myomectomy clamp should be applied from the front at about the level of the internal os, and its grasp should include the round ligaments, for otherwise there is a tendency for the jaws of the clamp to slip downward below the uterine arteries. The clamp should not be removed until the suturing is complete. On taking it off the uterus flushes up like a limb after the removal of a tourniquet, but the flushing is temporary and subsides in a few minutes.

As regards the incision in the uterus this should be anterior and central whenever possible. Tumors lying off the middle line can be reached by secondary incisions starting from the primary incision and tunneling outward. Tumors lying in the posterior wall if not too large are to be removed "transcavity," the lumen of the uterus being opened from the front and the posterior wall being incised through the posterior endometrium.

There is no risk in opening the uterine cavity, and it has the advantage of preventing small submucous fibroids or mucous polyps being overlooked, while palpation

of the uterine wall for seedlings is best carried out with one finger in the cavity. Every fibroid down to the smallest seedling must be removed.

After the removal of a fibroid or fibroids a more or less hypertrophied uterus remains. Involution occurs as after labor but with less vigor, and the sutured organ when returned to the abdomen should not greatly exceed the normal in bulk. It is therefore necessary in most cases to cut away part of the redundant uterine wall before suturing it.

A large fibroid growing in the posterior uterine wall should be dealt with by what I call the "Hood Operation." A transverse incision is made extending from just behind the tubouterine junction on one side to a corresponding point on the other side. The incision should open the capsule of the tumor and through it the tumor should be extracted by morcellation, so as to avoid extending the primary incision by tearing it outward. The morcellation being completed a "hood" composed of the posterior uterine wall superficial to the tumor is left behind. This if too thick and stiff must be first "planed down" by the scalpel and then brought over the fundus by a series of buried sutures until the final suture line lies in a horseshoe curve on the front of the uterus with the lowest placed suture just above the bottom of the uterovesical growth.

This is a satisfactory operation to perform and leaves a perfectly smooth and normal posterior uterine wall opposed to the intestines, whereas if the fibroid is removed via an incision through the posterior wall, a suture line is left directly inviting intestinal adhesion.

There are some cases in which the number of the fibroids to be removed is too great to allow of either of the two former methods being applied. In such I perform what I call "block excision." The uterus is first bisected down nearly to the internal os. The index finger is now inserted into each cornu in turn to mark their positions, and these being defined a wedge-shaped excision is carried out on each side with its base at the fundus and its apex below. In cutting the wedge the scalpel goes through any fibroid that may be in the line of the incision. It is necessary to be certain that the cornu is not cut away in doing this, and it is for this reason that the uterus is first bisected and the positions of the cornua defined by the finger tip.

The two much reduced halves of the uterus contain fibroids that have escaped the block excision. These are enucleated and the two halves are sutured together so that the strips of endometrium on either side reconstitute the uterine cavity with its cornual extensions. This operation has the drawback of leaving a suture line on the back of the uterus.

There is another class of case to which the ordinary technic of myomectomy is unsuited, namely, cases of cervical fibroids. The myomectomy clamp cannot be applied in these cases until the tumor is enucleated, but the circulation through the ovariopelvic ligaments should be controlled. The uterus is then bisected until the capsule of the tumor is opened and the tumor is then enucleated. An immensely redundant supravaginal cervix remains. This can be reduced in circumference by cutting away sufficient of the cervical wall. Before starting to do this a long narrow pressure forceps or strong probe should be pushed down the cervical canal to indicate its position, otherwise it is in danger of being cut away. The halves of the body of the uterus and the cervix are now sutured together leaving a very long cervix with the body perched up on the top of it. This condition should be dealt with by performing the Baldy-Webster operation which acutely anteflexes the uterus and the upper part of the cervix. As involution proceeds the length of the cervix will attain the normal.

Finally, as regards the suture of the enucleation cavities: a very reliable and strong catgut should be used and mattress sutures should be avoided because they tend to obstruct the blood supply. For inserting the sutures the pattern of

Reverdin's needle that I use is superior to ordinary needles because its great strength allows its being passed round cavities without fear of breakage.

It has been suggested that the uterine vessels may be damaged by the myomectomy clamp with consequent risk of embolism. It is not so; no damage is done to them. Of the seven deaths I record, two were due to pulmonary embolism, but these occurred among my early cases, before I began to use the myomectomy clamp.

7. When Is Surgery Indicated in Retrodisplacement of the Uterus?

Dr. George H. Gardner, Chicago, Ill. (For original article, see page 596, October issue.)

DISCUSSION

DR. GERALD C. MELHADO, MONTREAL, CANADA (by invitation).—In considering "backward displacements" of the uterus, it is necessary to bear in mind that the uterus is essentially a specialized part of the pelvic floor, and that, within the limits of the normal position, it is permitted a wide range of movement.

The term "backward displacement" of the uterus has come to include not only variations in the position of the uterus, but also in the direction of its axis, and even of its component parts.

I believe that there is a great difference between mobile and fixed retroversion. In Dr. Gardner's series of 145 cases, he classifies 83 as essential retrodisplacements, only 9 of which were unassociated with any pathologic lesion in the pelvis. Of the 62 incidental cases, all were associated with some complicating pelvic disease. It may therefore be justifiably claimed that the associated lesions were the predominant cause of symptoms and the underlying factor for surgical intervention, the retrodisplacement playing only a minor part if any. Whether retrodisplacement may be said to be the cause of the associated lesions is, however, another story.

In the Gynecologic Department of McGill University it was taught that the normal position of the uterus was in the principal axis of the pelvis, with the cervix at the level of the ischial spines, and the fundus slightly forward of the pelvic axis; i.e., slightly anteverted and anteflexed, but that in 25 per cent of healthy women the uterus was retroverted, and that this position caused no symptoms and required no treatment.

It is undeniable that the retroverted uterus is placed at a disadvantage in the pelvis, and is subject to the intestinal and intraabdominal pressure acting directly on the uterus, and, so, is a predisposing cause of a prolapse; in fact, *it is the* first stage of a prolapse. It is in this prolapse that the importance of the condition lies, for it is this prolapse and not the retroversion which gives rise to the symptoms.

In the matter of symptoms and signs, it may be fairly said that their presence is in no sense a characteristic of retroversion, or any other displacement, and so the displacement may be but a coincidence, and possess no etiologic factor whatever.

The ovaries in retroversion, however, are specially liable to prolapse, and so exert a downward traction upon their special attachments. They then may become edematous, hypertrophic, or undergo degenerative changes and add their weight to the uterus. They may sink down into the pouch of Douglas and underlie the uterus. A tuboovarian varicocele, especially marked in the pampiniform plexus, may occur. We have had several such cases.

After a careful review of 261 cases of retroversion, occurring in the Royal Victoria Hospital during the past five years, and searching for the cause of symptoms, I was unable to conclude that the retroversion per se would account for them, and was forced to attribute them to a variety of associated lesions.

Again, menstrual disturbances have not been observed as being present where the uterus was maintained at its proper level in the pelvis. It has been noted, however, that, although retroversion of the uterus cannot be said to be *the* underlying factor

in causing sterility, nevertheless pregnancy has rapidly followed the simple procedure of lifting forward the body of the uterus and so making it possible for the cervix to lie in the seminal lake.

When general treatment fails and the retroversion is associated with some prolapse, a suspension operation is possibly justifiable as part of the corrective measure. The method most frequently used in the Royal Victoria Hospital is the Olshausen suspension, closing off the lateral apertures by stitching the round ligament to the anterior abdominal wall, thus preventing a possible hernia of the small bowel.

DR. HAROLD O. JONES, CHICAGO, ILL.—Our experience is parallel to that of Dr. Gardner in that the majority of patients in our clinic have been operated upon for the complication rather than for the retrodisplacement per se.

Those patients who have had defundation of the uterus have also had complications. Our greatest number were in those cases done abdominally; in our experience we had considerably fewer in those done by the vaginal route.

Our technical procedure has also paralleled that of Dr. Gardner. We follow his technic in detail. In years gone by I personally had the privilege of delivering twelve patients who had this type of operation and there was no great delay in delivery. In the patients examined subsequently there was no return of the retrodisplacement.

DR. ARTHUR H. CURTIS, CHICAGO, ILL.—In one of the group of patients just referred to upon whom I operated, death resulted from pulmonary embolus. The patient was a young woman with marked varicosities of the broad ligament veins. There were present in the operating room some six or eight guests and I am always disposed to demonstrate all of the pathology present. I lifted the uterus a distance of 8 or 9 inches to show its marked mobility, and turned it from side to side perhaps as many as four or five different times. The patient's recovery was uneventful until about the tenth day, when she had a most excruciating backache. This happened during the night and I appreciated the possibility of there being a thrombosis. She seemed well the next morning, then died suddenly with typical embolic symptoms. Since that time, I have preached to our students and associates that it behooves us to be painstakingly careful in manipulating an unduly mobile uterus, especially in the presence of dilated pelvic veins.

DR. JOSEPH L. BAER, CHICAGO, ILL.—I would call attention to the work of Sturmdorf on causes of retrodisplacement, such as differences in pelvic inclination and the effect of intraabdominal pressure on the uterus in early infancy. I think it may be accepted that in the patient in whom there is little pelvic inclination and in whom the top of the symphysis and the promontory are almost on a parallel, that that patient is going to have a retrodisplacement in adult life which in her is a part of her normal state. However, she is most likely to have the disorders that may follow in the subsequent course of the retrodisplacement.

DR. WILLIAM C. DANFORTH, EVANSTON, ILL.—In addition to a considerably larger number done earlier, I have recently seen five women operated upon by the technic which has been described, four of whom have passed through pregnancy and labor, one of them for the second time. The fifth is now pregnant. In all of these the uterus has remained in the position at which it was left at the time of operation.

Dr. Gardner spoke of the effect of retrodisplacement as a cause of sterility. I feel that retrodisplacement may be an occasional cause of sterility, but I think it is not a very frequent one because I see each year a number of women who have retrodisplacement and who are pregnant. Some of these have been pregnant a number of times. In an analysis made several years ago of 1,000 private cases to determine the incidence of retrodisplacement in pregnancy and the puerperium, we found a little over 18 per cent of retrodisplacements.

(To be continued in the December issue.)

NEW YORK OBSTETRICAL SOCIETY

MEETING OF FEBRUARY 12, 1935

The following paper was presented:

The Treatment of Vesicovaginal Fistulas: Past and Present. Dr. Norman F. Miller. (By invitation. For original article, see page 675.)

MEETING OF MARCH 12, 1935

The following papers and case reports were presented:

Primary Carcinoma of the Fallopian Tube. Dr. W. T. Dannreuther. (For original article see page 724.)

Histologic and Hormonal Studies in Chronic Mastitis. Dr. Howard C. Taylor, Jr.

The Histogenesis of Some Ovarian Tumors and Their Biologic Effect. Dr. S. H. Geist. (For original article, see page 650.)

OBSTETRICAL SOCIETY OF PHILADELPHIA

MEETING OF MAY 2, 1935

The following paper and case report were presented:

Hematometra. Dr. John A. McGlinn and W. Benson Harer. (For original article, see page 704.)

Chorionepithelioma Following Full-Term Pregnancy. Dr. Clifford B. Lull. (For original article, see page 730.)

CHICAGO GYNECOLOGICAL SOCIETY

MEETING OF MAY 17, 1935

The following papers were presented:

The Toxemias of Late Pregnancy. Drs. W. A. Thomas, E. D. Allen, C.P. Bauer, and M. R. Freeland. (For original article, see page 665.)

Out-Patient Obstetrics. Dr. Henry Buxbaum. (This paper will appear in the December issue.)

Brenner Tumor of the Ovary. Dr. Philip H. Smith. (For original article, see page 734.)

Tubal Reimplantation—In Retrospect. Dr. George de Tarnowsky. (For original article, see page 696.)

Monoamniotic Twins, One Normal, the Other Anencephalic; Multiple True Knots in the Cords. Drs. Sol Litt and Herman A. Strauss. (For original article, see page 728.)

BROOKLYN GYNECOLOGICAL SOCIETY

MEETING OF APRIL 5, 1935

The following case report and paper were presented:

Spontaneous Evolution of a Transverse Presentation. Dr. William G. Fraser (by invitation). (For original article, see page 732.)

Some New Aspects of the Menstrual Problem. Dr. Carl G. Hartmann (by invitation).

Department of Book Reviews

Conducted by Robert T. Frank

Review of New Books

Gynecology and Obstetrics

The progress in gynecology which has taken place during the twelve years since the first edition of Dr. Anspach's book, *Gynecology*,[1] was published, has required numerous additions, corrections and modifications of the subject matter in the subsequent editions called for by the popularity of this work. The fifth edition has now been entirely rewritten and appears as a new book. The additions apply particularly to the sections dealing with physiology, disturbances of function, radiation treatment, endometriosis, and several others. The assistance of a number of collaborators, specialists in their various fields are acknowledged and the present edition, as have the others, affords an up-to-date knowledge of this important branch of medicine.

—*George W. Kosmak*

The difficulty in preparing a text suitable at once in elementary principles for the student, in presentation of symptomatology, diagnosis, and treatment for the general practitioner, and in offering surgical methods tried by years of experience and judgment for the operator has been overcome in Curtis' *Textbook of Gynecology*.[2] In this second edition marked by an absence of debate, a conciseness of diction, a fullness of detail where necessary, and an abundance of beautifully executed illustrations portraying carefully selected operative maneuvers, one finds a well-balanced exposition of present-day American gynecologic teaching which may be heartily recommended.

—*Philip F. Williams*

In this second edition of *Practical Surgery of the Abdominal and Pelvic Regions*,[3] Dr. Kennedy brings out the constructive principles underlying the surgical teachings of his late chief, Dr. Joseph Price. Departing from time-honored custom the author follows no rule as to order of subject matter nor of arrangement as to the pathologic lesion treated but considers all phases of pelvic disease under the operation by which they may be, in his opinion, best handled.

---

[1] **Gynecology.** By Brooke M. Anspach, M.D. Fifth Edition. Re-illustrated and completely revised by the author with the assistance of Philip F. Williams, M.D. and Lewis C. Scheffey, M.D. J. B. Lippincott Company, Philadelphia, Pa., 1934.

[2] **Textbook of Gynecology.** By Arthur Hale Curtis, Professor and Head of Department of Obstetrics and Gynecology, Northwestern University Medical School, etc. Second edition, with 300 illustrations, and 493 pages. W. B. Saunders Company, Philadelphia, 1934.

[3] **Practical Surgery of the Abdominal and Pelvic Regions.** By James William Kennedy, Surgeon-in-Chief to the Joseph Price Hospital, etc. Second edition, illustrated with 133 original half-tone plates, some in color, and 861 pages. F. A. Davis Company, Philadelphia, 1934.

In the first chapter vaginal hysterectomy is described in fullest detail as to indication and technic. Dr. Kennedy states he would feel no apology needed for the appearance of this volume if he could influence a trend toward more frequent use of vaginal hysterectomy. Of particular interest among the other chapters are those discussing the handling of suppurative adnexal lesions and pelvic peritonitis; undoubtedly objection may be raised to the reasoning involved in the discussion of these subjects. The volume closes with a recollection of Dr. Price's personality and sayings.

—*Philip F. Williams*

Béclère prefaces this monograph on *Roentgen Treatment of Uterine Fibromas and Metropathies*[4] with a short and interesting history of the stages of the treatment of the fibromyomatous uterus. Gibert recounts here his experience in the L' Hopital Saint-Antoine over a period of fourteen years in the roentgen therapy of fibroids and benign uterine hemorrhage. He brings out all the points of argument advanced, by the surgically inclined, against the methods, which he naturally enough seeks to refute; and the evidence in favor of this treatment, which he supports. He lays stress, however, upon the exact indications for the selection of the method and is meticulous in discussing its limitations, and the possible complications and accidents which may arise in wrongly chosen cases. In his experience he has seen but four carcinomas, two of them cervix and two of them fundus, follow roentgen treatment of the two conditions named.

In the statistical review of 350 cases, 310 followed up, five failures were due to submucous fibroids. These were cured by surgical intervention. Three ovarian cysts treated by error in diagnosis were later cured by surgery.

Gibert concludes that roentgen therapy, properly used, is superior to both radium and surgery in the treatment of myomas and benign uterine bleeding.

—*Philip F. Williams*

The warm reception accorded two previous monographs, "Indication" and "Diagnosis," has prompted Benthin to prepare a third book on *Treatment in Gynecology*.[5] The author feels that in regard to completeness of presentation and economy, in comparison to the cost of the expensive systems, much can be gained for the profession by this manner of presenting the various phases of gynecology.

In addition to discussing the treatment of the diseases and functional and organic alterations of the pelvic organs there are included chapters relating to the breast, the abdominal wall, the intestine and urinary tract, and contraceptive methods. Minor gynecologic surgical methods receive attention as to indications and usefulness. The subject of heat and other physical agents is briefly discussed. In regard to gynecologic manifestations of endocrine diseases, Benthin thinks that no outstanding results have been obtained by biologic therapy and feels that many apparent successes are due as much to general therapy as to the hormone used.

This monograph is comprehensive as to topics covered and well detailed as to ambulatory treatment and methods.

—*Philip F. Williams*

---

[4]**La Roentgenthérapie des Fibromyomes de l'uterus, et de metropathies hemorragigues.** Par Paul Gibert. Avec 10 figures dans le texte, et 110 pages. Masson et Cie. Editeurs. Paris, 1935.

[5]**Therapie der Frauenkrankheiten.** Von Professor Dr. W. Benthin, Koenigsberg i. P. Mit 23 Abbildungen im Text. Verlag von Urban und Schwarzenberg, Berlin und Wien, 1934

This book designed primarily for the general practitioner is a guide to the *Treatment of Common Female Ailments*[6] and has been very well brought up to date in this edition. There have been added ten new chapters including examination, the endocrine glands, menopause, perineal injuries, gastrointestinal ailments, fertility, sterility, and especially two chapters on the Prevention of Female Ailments.

The brevity of some of the material is more than made up for in the succinctness and the common sense discussion of the subjects. While emphasis has been laid upon symptoms and diagnosis, the value of the book to the practitioner is increased through the detailed discussion of treatment of minor conditions which may be handled in office practice, as well as suggestive prescriptions.

The author does not advocate glandular therapy in endocrine disturbances, although he gives an excellent review of the present status of the principles involved. The chapters on postoperative care, postnatal treatment and prevention of female ailments contain some very fine ideas on gynecologic prophylaxis. The book is highly recommended to the general practitioner.

—*Philip F. Williams*

The large number of individual studies of biochemic changes in the course of the various phases of reproduction call for just such a comprehensive and critical review as is offered in this small monograph entitled *Physiologic Chemistry at Birth.*[7] Adding to already available information the results of his own extensive investigations, the author arrives at the interesting conclusion that the process of birth in regard to chemical and physicochemical changes does not represent a unity but must be divided into four parts: Dilatation of cervix; main part of expulsion stage; actual expulsion of child, and postpartum period. The characteristics of biochemic alterations for each of these four stages are described in detail. This monograph will be of outstanding value particularly to scientific workers in this special field.

—*Hugo Ehrenfest*

This book reflects the heightened interest of recent years in *Obstetrical Analgesia and Anesthesia.*[8] The author through her hospital affiliations and experience is well qualified to write authoritatively on the subject.

The methods applicable to the various stages of labor, abnormal deliveries and complicated labors are described in detail as to choice, action, and dosage of the agents and technic. There is a timely and important section upon resuscitation of the newborn where asphyxia has resulted from the drugs administered. The applicability of the various methods of analgesia and anesthesia to house practice is fully discussed.

That the dosage of some drugs has been calculated upon the English system of weights, stones, and pounds, does not lend the tables to universal use. The adoption of a parallel metric system might have been in order. Many American obstetricians question the suggested use of morphine shortly before delivery, others do not favor the recommended wide use of spinal anesthesia in cesarean section,

---

[6]**Treatment of Common Female Ailments.** By Frederick John McCann, Consulting Surgeon, Samaritan Free Hospital for Women, London, etc. Third edition. 379 pages. William Wood & Co., Baltimore, 1934.

[7]**Die Physiologische Chemie der Geburt.** Von Dr. Heinz Siedentopf, Privatdozent fuer Geburtshilfe und Gynaekologie an der Universitaet Leipzig. Pp. 130. Mit 5 Kurven und 21 Tabellen. Johann Ambrosius Barth, Leipzig, 1932.

[8]**Anaesthesia and Analgesia in Labour.** By Katharine G. Lloyd-Williams, M.D., Honorary Anaesthetist to the Royal Free Hospital in London, etc. With foreword by Dame Louise McIlroy, Professor of Obstetrics and Gynaecology, London School of Medicine for Women. 96 pages. William Wood & Co., Baltimore, 1934.

while others would regard the omission of mention of local anesthesia in the section dealing with toxemias a serious fault in the presentation of the subject.

Otherwise there is very much worth while in this full, though concise, analysis of the various methods of analgesia and anesthesia.

—*Philip F. Williams*

Miscellaneous

The author of *Economic Problems of Medicine*[9] was a signer of the minority report of the Committee on the Costs of Medical Care. He subjects the social and economic problems of medicine to a critical analysis in a series of topical discussions and brings out strongly the rights of the physician in the presently changing methods of practice.

His ideas regarding the socialistic merger of Medicine with a machine-age type of practice will be shared by all intelligent physicians. He presents some remarkable figures regarding the extent of present hospital facilities and indicates a reduction of their cost. The obligation of the physician to the medical organizations stresses the effect of collective action in many health problems. The relation of the physician to the community should be to preserve the personal relation of physician and patient. The author vigorously upholds the recommendations of the minority group who discussed the medical care of the American people.

There is a careful analysis of the various present and proposed systems and schemes of compensation and health insurance, foreign and domestic, and the subject of industrial medicine is fully covered. The newer methods of medical and dental care as worked out locally in various areas are dissected and discussed. The author indicates that no one plan may be feasible in all districts. He describes the possible developments which may ensure health to the nation and position and progress for the medical profession. The book should be widely read.

—*Philip F. Williams*

A Committee of the Western Surgical Association has compiled a list of the *Names of Surgical Operations*.[10] This nomenclature greatly reduces the multiplicity of names of surgical operations and has dropped the eponymic terminology in favor of a common sense anatomic term describing the procedure employed. The classification provides not only for uniformity, but allows for a flexibility found in an advancing science, and a continuity of the system may be provided by periodic revisions.

The names of operations are listed by system. At the foot of each page is a set of qualifying words and phrases which may be added to the names of surgical operations. There is an appendix listing fundamental surgical procedures, another discussing philologic suggestions and corrections, for some criticisms will be made by the purists, and a final appendix on commonly used suffixes.

The original number of operations listed and sent out for correction was 3,313. The number was thus reduced to the 743 titles given. This reduction of 75 per cent of the bulk of words and phrases used in the present recording of surgical procedures is praiseworthy. An example of this reduction which should be of interest to all gynecologists is given on pages eight et seq. where a list of sixteen

[9]**Economic Problems of Medicine.** By A. C. Christie, M.S., M.D., Professor of Clinical Radiology, Georgetown University, Medical School, etc. 242 pages. The Macmillan Company, New York, 1935.

[10]**Names of Surgical Operations.** Compiled and arranged by the Western Surgical Association through its Special Committee. Edited by Carl E. Black, A.M., M.D. 102 pages. Bruce Publishing Co., St. Paul, Minn., 1935.

operations, the majority of the titles eponymic, have been reduced in the present system to two operations. It is apparent that some alterations and additions should be made in the list of names of obstetric operations. In the index, one finds 103 operations listed under delivery; under uterus, 26 procedures are listed.

Such a list will be to surgical records of the future what the Basle Nomenclature is to anatomy and what the new Standard Nomenclature of Diseases is to the record filing room. This list deserves the adoption and warm support of all surgical clinics. The Editor requests corrections, criticisms, and other suggestions.

—*Philip F. Williams*

This book entitled *Dynamics of Population*[11] represents an extended inquiry into certain social and demographic data which bear upon the reproduction trends and other differentials in the various racial and cultural groups which make up our national population.

The population growth in the United States is slowing down. The authors of this study feel that an equilibrium will be reached in from twenty to forty years with a maximum population of some 150 million or less. The trends of social and genetic heritage responsible for the decrease have been analyzed, with a study of the by-effects of communal resistance or expansion, and economic status as modifying influence on the above factors. A study of the fertility and reproduction differentials in these groups leads the authors to feel there will be little probability of any levelling of or reversals of these differentials.

The measurable characteristics of American groups especially as regards health and cultural-intellectual development when studied from various available documented sources showed a constant finding of high frequency of individual ability in the upper social classes. However trite this conclusion may sound, the observations which lead to it form an intensely interesting survey of our socio-economic and occupational groups.

The final section of the book on the causes and control of population trend brings out many factors which will merit the attention of eugenists and those of the profession who may be interested in the broader aspects of fertility, sterility, and the control of reproduction. With candor and without bias the physical and medical, as well as the economic and social, factors affecting fertility are reviewed. Such remedies for the avoidance or correction of the factors resulting in unfavorable differentials in the birth rate are discussed in the final chapter on social control. One feels the broadminded attitude of the authors toward the whole subject of social control epitomized in the section "conditions affecting the economic security of young couples."

There are various appendices of supporting material, a glossary and a documentation of sources of material. To the eugenist, the student of society, and the physicians this book will be of great interest and value. To the obstetrician it brings in another manner to our attention what Litzenberg has termed, "the challenge of the falling birth rate."

—*Philip F. Williams*

This volume is intended to cover the whole subject of *Birth Control*[12] for the general public. The author has admirably succeeded in her task. No longer a

---

[11] **Dynamics of Population.** By Frank Lorimer and Frederick Asborn. The Macmillan Company, New York, 1934.

[12] **Birth Control. Its Use and Misuse.** By Dorothy Dunbar Bromley, with an introduction by Dr. Robert Latou Dickinson. 304 pages. Harper & Brothers, New York, 1934.

controversial topic but a living issue forced upon us by economic circumstances it is timely that such a complete and sanely written discussion for the laity on control of births has appeared.

The various methods of contraception, ancient and modern, natural and mechanical are described. The fallacy of the low risk period of the Ogino-Knauss theory is exploded. The reluctant attitude of organized medicine to have the archaic Comstockian Federal and State laws revised is fittingly chided. The illegal abortion problem in this country and the legal abortion problem in the Soviet area are well handled. The author's references show very certainly that legalized abortion is no solution to the problem of birth control. There is a chapter on sterilization and one on sterility which are quite in place in a book of this nature. A very extensive recent bibliography and a résumé of the State laws on contraception complete the book.

—Philip F. Williams

The jacket of this book[13] contains the statement that due to existing laws regarding the dissemination of *information upon birth control* this volume is to be sold only to physicians or upon a physician's prescription. This is rather an anomaly when one realizes the enormous amount of thinly veiled literature distributed openly upon feminine hygiene in the United States today.

In this small volume Fielding discusses the methods he has found of most value in his work in England. He makes a very good case for birth control in his clear chapters on the sociologic factors and meaning of the movement to free this branch of medicine from its present legal shackles. He ably refutes many of the objections to an open knowledge of the subject by the public and the instruction of the laity by physicians on birth control methods.

—Philip F. Williams

In a remarkable series of sixty-four photographic studies, Killian has portrayed the *Facial Expressions of Pain*[14] observed in a large variety of diseases. Technically the work was accomplished in natural light with a Rolliflex camera, yellow filter, and superpan film. The result of his labors is an outstanding contribution to photography in clinical medicine. The changes shown in the face during the progress of a case of juvenile sarcoma, and of a case of tuberculous peritonitis are more striking evidence of the advance of the disease than any progress notes could ever be.

Killian pleads for a more extended use of the camera in recording the ravages of the disease not only upon the physical make-up of the face but also upon its superphysical or spiritual embodiment. He feels that in this way physicians may be trained to a greater degree in the art of observation of emotional and psychical manifestations of disease as contrasted with the somatic alterations of the countenance.

—Philip F. Williams

The thin paper and small type used has permitted a great deal more material to be included in this small book on *Genitourinary Diseases*[15] than its size would indicate. In the first four chapters the text offers the essential principles govern-

---

[13]**Parenthood. Design or Accident? A Manual of Birth-Control.** By Michael Fielding, M.D. With 8 illustrations, and 239 pages. The Vanguard Press, New York, 1935.

[14]**Facies Dolorosa. Das Schmerzliche Antlitz.** Von Dr. H. Killian. Mit 64 Abbildungen. 88 pages. Verlag von Georg Thieme, Leipzig, 1934.

[15]**Synopsis of Genitourinary Diseases.** By Austin I. Dobson, Professor of Genitourinary Surgery, Medical College of Virginia. With 111 illustrations. The C. V. Mosby Co., St. Louis, 1934.

ing diagnosis, examination, anatomy, and anomalies. Following this the separate diseases and conditions of the urologic tract are considered seriatim. While lacking the full detail of a larger text, the book offers a sufficient discussion as to diagnosis and treatment to be of much value to the physician in general practice.

—Philip F. Williams

The author presents this book as the result of his researches into the manifestations of the relation of *rheumatism and disorders of the autonomic nervous systems*[16] to various organic and systemic diseases.

In considering the female reproductive system in regard to this relationship he discusses two types of dysmenorrhea, the hypertensive and the hypotensive. The former he feels is due to a hyperaugmentation of the uterine os through the thoracicolumbar system, the latter is due to a contraction of the body of the uterus. The stimulating causes are mental, toxic, and allergic. Menorrhagia he regards as due to an imbalance of the autonomic system. This may appear through either excessive inhibiting action or through deficient augmentatory action of both systems. In pregnancy the hypertonic, excessive augmentative action of the thoracicolumbar system, causes slow dilatation of the cervix, and a tendency to toxemia; the opposing or opposite system predisposes toward relaxation, easy labors and hemorrhage from a lack of pressor influences.

Whether all the author's theories in regard to arthritis and other joint conditions will be accepted remains to be seen.

—Philip F. Williams

[16]**The Autonomic Diseases or Rheumatic Syndrome.** By Dr. T. M. Rivers. 299 pages. Dorrance & Company, Inc., Philadelphia, 1934.

Items

ANNOUNCEMENT

During the Spring of 1935 a committee for the study of sex variants was formed with the following membership: Chairman, Eugene Kahn, M.D., Yale University; Secretary, Robert W. Laidlaw, M.D., Columbia University; Treasurer, Carney Landis, Ph.D., Columbia University. These three officers, together with Robert L. Dickinson, M.D., National Committee on Maternal Health, and Josephine H. Kenyon, M.D., Columbia University, constitute the Executive Committee. The Committee members are Clarence O. Cheney, M.D., Columbia University; Maurice R. Davie, Ph.D., Yale University; Earl T. Engle, Ph.D., Columbia University; George W. Henry, M.D., Cornell University; E. A. Hooton, Ph.D., Harvard University; Marion E. Kenworthy, M.D., New York School of Social Research; K. S. Lashley, Ph.D., Harvard University; Adolf Meyer, M.D., Johns Hopkins University; Catharine Cox Miles, Ph.D., Yale University; Harold D. Palmer, M.D., University of Pennsylvania; Philip E. Smith, Ph.D., Columbia University; Edward A. Strecker, M.D., University of Pennsylvania; Lewis M. Terman, Ph.D., Stanford University; and Dorothy S. Thomas, Ph.D., Yale University.

The objects and reasons for the organization of this Committee are the following:

1. To correlate the various scientific interests in this field of study.
2. To serve as a scientific sponsoring agency for the furtherance of research on sexual variation.
3. To appoint advisory sub-committeees for projects sponsored or to be sponsored by the Committee.

At the present time the Committee is sponsoring several projects dealing with homosexuality as it appears in various classes of society. A study of 50 male and 50 female homosexuals of cultured background is already under way. Plans are far advanced for: (1) A study of homosexuality as it exists among members of the U. S. Marine Corps; and (2) A study of homosexual practices among adolescent boys who are inmates of an institution for juvenile delinquency. These projects include a psychiatric, endocrinological, roentgenological and hormonal approach to the problem.

The Committee will be glad to consider any research projects which may be presented that have a bearing upon the physiological, psychological, psychiatric or sociological problems of sex variants, and to act in a sponsoring and advisory capacity should such projects be approved.

All communications should be addressed to the Secretary, Dr. R. M. Laidlow, at 199 Fort Washington Avenue, New York City.

American Board of Obstetrics and Gynecology Examination

The next written examination and review of case histories of Group B applicants for certification by this Board will be held in various cities of the United States and Canada on Saturday, December 7, 1935.

Application blanks and booklet of information may be obtained from Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh (6), Pennsylvania. Applications for this examination must be filed in this office not later than November 1, 1935.

American Association of Obstetricians, Gynecologists and Abdominal Surgeons

At the last Annual Meeting of the Association, held September 16, 17, and 18, of the current year, the following officers were elected:

Dr. Louis E. Phaneuf, President
Dr. James W. Kennedy, President-elect
Dr. F. H. Falls, Vice President
Dr. Lewis F. Smead, Treasurer
Dr. James R. Bloss, Secretary
Dr. Leroy A. Calkins, Assistant Secretary
Dr. W. T. Dannreuther and Dr. M. Pierce Rucker, members of the Executive Council.

The Central Association of Obstetricians and Gynecologists

The Seventh Annual Meeting of the Central Association of Obstetricians and Gynecologists was held in Omaha, October 10, 11, and 12. The guest speaker was Dr. Walter T. Dannreuther of New York. The following officers were elected:

President, Dr. Buford G. Hamilton, Kansas City, Mo.
President-elect, Dr. Jeane Paul Pratt, Detroit, Mich.
Vice President, Dr. James R. Garber, Birmingham, Ala.
Secretary-Treasurer, Dr. Ralph A. Reis, Chicago, Ill.

Detroit was chosen as the meeting place for 1936.

Errata

In Dr. Samuel H. Geist's article in the October issue of the JOURNAL on page 483, the legend for Fig. 4 should read "Lipoid stain showing presence of fat globules in the tumor cells." Also on page 490, the legend for Fig. 14 should read "Showing connective tissue arrangement with fine fibrils extending into the cellular islands and surrounding the individual cells."

The author of an article entitled: Maternal Morbidity and Mortality in the Philippine General Hospital, abstracted in our JOURNAL 29: 239, 1935, is Dr. H. Acosta-Sison.

On page 447 of the September issue of the JOURNAL in footnote 19 the title of the book should read "Healthy Babies Are Happy Babies".

Books Received

THE STORY OF MEDICINE IN THE MIDDLE AGES. By David Riesman, M.D., Sc.D., Professor of History of Medicine and Professor Emeritus of Clinical Medicine, University of Pennsylvania, etc. Illustrated. 402 pages. Paul B. Hoeber, Inc., New York, 1935.

THEORY AND PRACTICE OF ANESTHESIA. By M. D. Nosworthy, M.D., Anaesthetist to Westminster Hospital, Grosvenor Hospital for Women, etc. With 35 illustrations, 224 pages. Hutchinson's Scientific Publications, London, E.C.4., 1935.

GYNECOLOGICAL AND OBSTETRICAL TUBERCULOSIS. By Edwin M. Jameson, M.D., Fellow of Trudeau Foundation, Attending Surgeon, Saranac Lake General Hospital, etc. Illustrated with 31 engravings, 256 pages. Lea & Febiger, Philadelphia, 1935.

MEN AND WOMEN. The World Journey of a Sexologist. By Magnus Hirschfeld. English version, illustrated, 325 pages. G. P. Putnam's Sons, New York, 1935.

YOUR NEW BABY. How to Prepare for It, How to Care for It. By Linda McClure Woods, R.N. Illustrated. Robert M. McBride & Co., New York, 1935.

MIDWIFERY. By Ten Teachers. Under the direction of Clifford White, M.D., F.R.C.P.(Lond.), F.R.C.S.(Eng.), etc. Edited by Sir Comyns Berkeley, J. S. Fairbairn and Clifford White. Fifth edition, illustrated, 740 pages. William Wood & Co., 1935.

ETUDOS CIRURGICOS. Par Eurico Branco Ribeiro. I. Serie. Pp. 241. Sociedade Editora Medica Limitada. São Paulo, Brasil, 1934.

PUERPERAL GYNECOLOGY. By J. L. Bubis, M.D., F.A.C.S., Consultant in Obstetrics, Gynecologist, Mt. Sinai Hospital, Cleveland, Ohio, etc. Illustrated, 199 pages. William Wood & Co., Baltimore, 1935.

PRINCIPLES AND PRACTICE OF MEDICINE. Originally written by the late Sir William Osler. Twelfth edition; revision made by Thomas McCrae, Professor of Medicine, Jefferson Medical College, Philadelphia. 1196 pages. D. Appleton-Century Co., New York, 1935.

PREVENTIVE MEDICINE AND HYGIENE. By Milton J. Rosenau, Professor of Preventive Medicine and Hygiene, Harvard Medical School. Sixth edition. D. Appleton-Century Company, New York, 1935.

LIFE BEGINS. Childbirth in Lore and in Literature. By Morris Braude, Associate Professor of Psychiatry, Rush Medical College, University of Chicago. 163 pages. Argus Books, Chicago.

OBSTETRICS for the General Practitioner. By J. P. Greenhill, Professor of Gynecology, Loyola University School of Medicine, Chicago. Edited by Morris Fishbein, M.D. 304 pages. National Medical Book Company, Inc., New York, 1935.

TRAITEMENT DE L'ECLAMPSIE. Par B. Stroganoff, Leningrad. Préface de H. Vignes. 112 pages. Masson et Cie, Paris, 1935.

THE OBSTETRIC PELVIS. By Herbert Thoms, Associate Professor of Obstetrics and Gynecology, School of Medicine, Yale University. With drawings and photographs by the author. 128 pages. Williams & Wilkins Company, Baltimore, 1935.

DISEASES OF WOMEN. By Harry Sturgeon Crossen, Professor Emeritus of Clinical Gynecology, Washington University School of Medicine, etc., and Robert James Crossen, Instructor in Clinical Gynecology and Obstetrics, Washington University School of Medicine, etc. Eighth edition, entirely revised and reset. With 1058 engravings, 999 pages. The C. V. Mosby Co., St. Louis, 1935.

INFANT NUTRITION. By William McKim Marriott, Professor of Pediatrics, Washington University School of Medicine. Second edition. The C. V. Mosby Co., St. Louis, 1935.

LEHRBUCH DER GEBURTSHILFE. Herausgegeben von Professor Dr. W. Stoeckel, Geh. Medizinalrat, Direktor der Universitaets-Frauenklinik in Berlin. Vierte, verbesserte Auflage, mit 620 zum groessten Teil farbigen Abbildungen im Text. 1036 pages. Verlag von Gustav Fischer, Jena, 1935.

OBSTETRICAL PRACTICE. By Alfred C. Beck, Professor of Obstetrics and Gynecology, Long Island College of Medicine, etc. With more than one thousand illustrations, 702 pages. Williams & Wilkins Company, Baltimore, 1935.

IMMUNOLOGY. By Noble Pierce Sherwood, Ph.D., M.D., Professor of Bacteriology, University of Kansas, and Pathologist of the Lawrence Memorial Hospital, Lawrence, Kansas. Illustrated, 608 pages. The C. V. Mosby Company, St. Louis, 1935.

THE PARATHYROIDS, in Health and in Disease. By David H. Shelling, M.D., The Johns Hopkins University and Hospital, Baltimore. Illustrated, 335 pages. The C. V. Mosby Company, St. Louis, 1935.

Witherspoon, J. Thornwell: Uterine Hemorrhage, A Simple and Practical Classification, New Orleans M. & S. J. **87**: 751, 1935.

The author offers a simple classification of common forms of irregular uterine bleeding based on the age of patients. Patients are divided into two groups: from 20 to 30, and from 40 upward. He realizes a difficulty in the intermediate group, 30 to 40 years, where the two groups overlap. In the younger group he lists (1) bleeding associated with some phase of pregnancy such as abortion and ectopic pregnancies, (2) acute pelvic infections, (3) endocrine disturbances, and (4) obstetric injuries (malpositions of the uterus, erosions, eversions, and lacerations). In the older group he lists in order of importance: (1) Cancer of the cervix and fundus, (2) hyperplasia of the endometrium, (3) submucous fibroids, (4) ovarian tumors, (5) cervical or uterine polyp.

The author emphasizes the fact that abnormal bleeding at the time of the menopause should be investigated by diagnostic curettage when the cause of the bleeding cannot be determined by other examination.

EUGENE S. AUER.